```
  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:36:41 ON 20 APR 2004

=> fil .bec
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS,
       ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 16:37:12 ON 20 APR 2004
ALL COPYRIGHTS AND RESTRICTIONS APPLY.  SEE HELP USAGETERMS FOR DETAILS.

11 FILES IN THE FILE LIST

=> s methionine and cysteine and muta?
FILE 'MEDLINE'
         42597 METHIONINE
         57135 CYSTEINE
        438717 MUTA?
L1         544 METHIONINE AND CYSTEINE AND MUTA?

FILE 'SCISEARCH'
         24318 METHIONINE
         40763 CYSTEINE
        419015 MUTA?
L2         349 METHIONINE AND CYSTEINE AND MUTA?

FILE 'LIFESCI'
         10146 METHIONINE
         16278 CYSTEINE
        197587 MUTA?
L3         189 METHIONINE AND CYSTEINE AND MUTA?

FILE 'BIOTECHDS'
          2902 METHIONINE
          3234 CYSTEINE
         37581 MUTA?
L4          101 METHIONINE AND CYSTEINE AND MUTA?

FILE 'BIOSIS'
         47747 METHIONINE
         53024 CYSTEINE
        490811 MUTA?
L5         471 METHIONINE AND CYSTEINE AND MUTA?

FILE 'EMBASE'
         30817 METHIONINE
         42800 CYSTEINE
        361935 MUTA?
L6         479 METHIONINE AND CYSTEINE AND MUTA?

FILE 'HCAPLUS'
         81396 METHIONINE
         89768 CYSTEINE
        448237 MUTA?
L7         967 METHIONINE AND CYSTEINE AND MUTA?

FILE 'NTIS'
           316 METHIONINE
           464 CYSTEINE
          9589 MUTA?
L8           0 METHIONINE AND CYSTEINE AND MUTA?
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FILE 'ESBIOBASE'
          7967 METHIONINE
         19691 CYSTEINE
        212411 MUTA?
L9         212 METHIONINE AND CYSTEINE AND MUTA?

FILE 'BIOTECHNO'
         12753 METHIONINE
         22339 CYSTEINE
        242571 MUTA?
L10        345 METHIONINE AND CYSTEINE AND MUTA?

FILE 'WPIDS'
          5145 METHIONINE
          6713 CYSTEINE
         24408 MUTA?
L11          83 METHIONINE AND CYSTEINE AND MUTA?

TOTAL FOR ALL FILES
L12       3740 METHIONINE AND CYSTEINE AND MUTA?

=> s l12 and oxidat?(3a)stab?
FILE 'MEDLINE'
        177858 OXIDAT?
        348673 STAB?
           765 OXIDAT?(3A)STAB?
L13          3 L1 AND OXIDAT?(3A)STAB?

FILE 'SCISEARCH'
        315112 OXIDAT?
        660640 STAB?
          4009 OXIDAT?(3A)STAB?
L14          3 L2 AND OXIDAT?(3A)STAB?

FILE 'LIFESCI'
         35638 OXIDAT?
        106043 STAB?
           202 OXIDAT?(3A)STAB?
L15          1 L3 AND OXIDAT?(3A)STAB?

FILE 'BIOTECHDS'
          8566 OXIDAT?
         33185 STAB?
           121 OXIDAT?(3A)STAB?
L16          2 L4 AND OXIDAT?(3A)STAB?

FILE 'BIOSIS'
        191044 OXIDAT?
        385436 STAB?
          1932 OXIDAT?(3A)STAB?
L17          1 L5 AND OXIDAT?(3A)STAB?

FILE 'EMBASE'
        151890 OXIDAT?
        330233 STAB?
           731 OXIDAT?(3A)STAB?
L18          1 L6 AND OXIDAT?(3A)STAB?

FILE 'HCAPLUS'
        551561 OXIDAT?
        677677 OXIDN
        931732 OXIDAT?
                 (OXIDAT? OR OXIDN)
       1376267 STAB?
```

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         16879 OXIDAT?(3A)STAB?
L19          8 L7 AND OXIDAT?(3A)STAB?

FILE 'NTIS'
         25321 OXIDAT?
        106510 STAB?
           623 OXIDAT?(3A)STAB?
L20          0 L8 AND OXIDAT?(3A)STAB?

FILE 'ESBIOBASE'
         61725 OXIDAT?
        142845 STAB?
           505 OXIDAT?(3A)STAB?
L21          0 L9 AND OXIDAT?(3A)STAB?

FILE 'BIOTECHNO'
         43160 OXIDAT?
        108410 STAB?
           262 OXIDAT?(3A)STAB?
L22          1 L10 AND OXIDAT?(3A)STAB?

FILE 'WPIDS'
        130044 OXIDAT?
         62050 OXIDN
            89 OXIDNS
        158499 OXIDAT?
                 (OXIDAT? OR OXIDN OR OXIDNS)
        716228 STAB?
          6351 OXIDAT?(3A)STAB?
L23          2 L11 AND OXIDAT?(3A)STAB?

TOTAL FOR ALL FILES
L24         22 L12 AND OXIDAT?(3A) STAB?

=> s sulfur free
FILE 'MEDLINE'
         33872 SULFUR
        418511 FREE
L25          69 SULFUR FREE
                 (SULFUR(W)FREE)

FILE 'SCISEARCH'
         73131 SULFUR
        513092 FREE
L26         173 SULFUR FREE
                 (SULFUR(W)FREE)

FILE 'LIFESCI'
          8227 "SULFUR"
         91913 "FREE"
L27          26 SULFUR FREE
                 ("SULFUR"(W)"FREE")

FILE 'BIOTECHDS'
          2279 SULFUR
         23610 FREE
L28          15 SULFUR FREE
                 (SULFUR(W)FREE)

FILE 'BIOSIS'
         55723 SULFUR
        432712 FREE
L29         100 SULFUR FREE
                 (SULFUR(W)FREE)
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FILE 'EMBASE'
         31784 "SULFUR"
        351213 "FREE"
L30          67 SULFUR FREE
                  ("SULFUR"(W)"FREE")

FILE 'HCAPLUS'
        321303 SULFUR
       1140806 FREE
L31         927 SULFUR FREE
                  (SULFUR(W)FREE)

FILE 'NTIS'
         26381 SULFUR
         58988 FREE
L32          64 SULFUR FREE
                  (SULFUR(W)FREE)

FILE 'ESBIOBASE'
          8161 SULFUR
        121030 FREE
L33          19 SULFUR FREE
                  (SULFUR(W)FREE)

FILE 'BIOTECHNO'
          7548 SULFUR
         81349 FREE
L34          26 SULFUR FREE
                  (SULFUR(W)FREE)

FILE 'WPIDS'
         22047 SULFUR
        477248 FREE
L35         104 SULFUR FREE
                  (SULFUR(W)FREE)

TOTAL FOR ALL FILES
L36        1590 SULFUR FREE

=> s l36 and l12
FILE 'MEDLINE'
L37          0 L25 AND L1

FILE 'SCISEARCH'
L38          0 L26 AND L2

FILE 'LIFESCI'
L39          0 L27 AND L3

FILE 'BIOTECHDS'
L40          0 L28 AND L4

FILE 'BIOSIS'
L41          0 L29 AND L5

FILE 'EMBASE'
L42          0 L30 AND L6

FILE 'HCAPLUS'
L43          2 L31 AND L7

FILE 'NTIS'
L44          0 L32 AND L8
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FILE 'ESBIOBASE'
L45           0 L33 AND L9

FILE 'BIOTECHNO'
L46           0 L34 AND L10

FILE 'WPIDS'
L47           0 L35 AND L11

TOTAL FOR ALL FILES
L48           2 L36 AND L12

=> s muta? and oxidat?(3a)stab?
FILE 'MEDLINE'
        438717 MUTA?
        177858 OXIDAT?
        348673 STAB?
           765 OXIDAT?(3A)STAB?
L49         49 MUTA? AND OXIDAT?(3A)STAB?

FILE 'SCISEARCH'
        419015 MUTA?
        315112 OXIDAT?
        660640 STAB?
          4009 OXIDAT?(3A)STAB?
L50         72 MUTA? AND OXIDAT?(3A)STAB?

FILE 'LIFESCI'
        197587 MUTA?
         35638 OXIDAT?
        106043 STAB?
           202 OXIDAT?(3A)STAB?
L51         35 MUTA? AND OXIDAT?(3A)STAB?

FILE 'BIOTECHDS'
         37581 MUTA?
          8566 OXIDAT?
         33185 STAB?
           121 OXIDAT?(3A)STAB?
L52         46 MUTA? AND OXIDAT?(3A)STAB?

FILE 'BIOSIS'
        490811 MUTA?
        191044 OXIDAT?
        385436 STAB?
          1932 OXIDAT?(3A)STAB?
L53         67 MUTA? AND OXIDAT?(3A)STAB?

FILE 'EMBASE'
        361935 MUTA?
        151890 OXIDAT?
        330233 STAB?
           731 OXIDAT?(3A)STAB?
L54         46 MUTA? AND OXIDAT?(3A)STAB?

FILE 'HCAPLUS'
        448237 MUTA?
        551561 OXIDAT?
        677677 OXIDN
        931732 OXIDAT?
                 (OXIDAT? OR OXIDN)
       1376267 STAB?
         16879 OXIDAT?(3A)STAB?
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L55         127 MUTA? AND OXIDAT?(3A)STAB?

FILE 'NTIS'
           9589 MUTA?
          25321 OXIDAT?
         106510 STAB?
            623 OXIDAT?(3A)STAB?
L56           0 MUTA? AND OXIDAT?(3A)STAB?

FILE 'ESBIOBASE'
         212411 MUTA?
          61725 OXIDAT?
         142845 STAB?
            505 OXIDAT?(3A)STAB?
L57           43 MUTA? AND OXIDAT?(3A)STAB?

FILE 'BIOTECHNO'
         242571 MUTA?
          43160 OXIDAT?
         108410 STAB?
            262 OXIDAT?(3A)STAB?
L58           35 MUTA? AND OXIDAT?(3A)STAB?

FILE 'WPIDS'
          24408 MUTA?
         130044 OXIDAT?
          62050 OXIDN
             89 OXIDNS
         158499 OXIDAT?
                  (OXIDAT? OR OXIDN OR OXIDNS)
         716228 STAB?
           6351 OXIDAT?(3A)STAB?
L59           47 MUTA? AND OXIDAT?(3A)STAB?

TOTAL FOR ALL FILES
L60          567 MUTA? AND OXIDAT?(3A) STAB?

=> s l36(5a)(protein# or enzyme#)
FILE 'MEDLINE'
        1616796 PROTEIN#
         688603 ENZYME#
L61           10 L25(5A)(PROTEIN# OR ENZYME#)

FILE 'SCISEARCH'
        1286946 PROTEIN#
         427906 ENZYME#
L62            6 L26(5A)(PROTEIN# OR ENZYME#)

FILE 'LIFESCI'
         491119 PROTEIN#
         189853 ENZYME#
L63            3 L27(5A)(PROTEIN# OR ENZYME#)

FILE 'BIOTECHDS'
         121281 PROTEIN#
         113032 ENZYME#
L64            0 L28(5A)(PROTEIN# OR ENZYME#)

FILE 'BIOSIS'
        1595193 PROTEIN#
         737412 ENZYME#
L65            8 L29(5A)(PROTEIN# OR ENZYME#)

FILE 'EMBASE'
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       1286373 PROTEIN#
        732081 ENZYME#
L66          5 L30(5A)(PROTEIN# OR ENZYME#)

FILE 'HCAPLUS'
       1870563 PROTEIN#
        884849 ENZYME#
L67         11 L31(5A)(PROTEIN# OR ENZYME#)

FILE 'NTIS'
         17507 PROTEIN#
         11889 ENZYME#
L68          0 L32(5A)(PROTEIN# OR ENZYME#)

FILE 'ESBIOBASE'
        588700 PROTEIN#
        205579 ENZYME#
L69          2 L33(5A)(PROTEIN# OR ENZYME#)

FILE 'BIOTECHNO'
        653195 PROTEIN#
        353854 ENZYME#
L70          2 L34(5A)(PROTEIN# OR ENZYME#)

FILE 'WPIDS'
        127697 PROTEIN#
         72171 ENZYME#
L71          1 L35(5A)(PROTEIN# OR ENZYME#)

TOTAL FOR ALL FILES
L72         48 L36(5A)(PROTEIN# OR ENZYME#)

=> s l36 and oxidat?(3a)stab?
FILE 'MEDLINE'
        177858 OXIDAT?
        348673 STAB?
           765 OXIDAT?(3A)STAB?
L73          0 L25 AND OXIDAT?(3A)STAB?

FILE 'SCISEARCH'
        315112 OXIDAT?
        660640 STAB?
          4009 OXIDAT?(3A)STAB?
L74          0 L26 AND OXIDAT?(3A)STAB?

FILE 'LIFESCI'
         35638 OXIDAT?
        106043 STAB?
           202 OXIDAT?(3A)STAB?
L75          0 L27 AND OXIDAT?(3A)STAB?

FILE 'BIOTECHDS'
          8566 OXIDAT?
         33185 STAB?
           121 OXIDAT?(3A)STAB?
L76          0 L28 AND OXIDAT?(3A)STAB?

FILE 'BIOSIS'
        191044 OXIDAT?
        385436 STAB?
          1932 OXIDAT?(3A)STAB?
L77          0 L29 AND OXIDAT?(3A)STAB?

FILE 'EMBASE'
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        151890 OXIDAT?
        330233 STAB?
           731 OXIDAT?(3A)STAB?
L78          0 L30 AND OXIDAT?(3A)STAB?

FILE 'HCAPLUS'
        551561 OXIDAT?
        677677 OXIDN
        931732 OXIDAT?
                 (OXIDAT? OR OXIDN)
       1376267 STAB?
         16879 OXIDAT?(3A)STAB?
L79          3 L31 AND OXIDAT?(3A)STAB?

FILE 'NTIS'
         25321 OXIDAT?
        106510 STAB?
           623 OXIDAT?(3A)STAB?
L80          1 L32 AND OXIDAT?(3A)STAB?

FILE 'ESBIOBASE'
         61725 OXIDAT?
        142845 STAB?
           505 OXIDAT?(3A)STAB?
L81          0 L33 AND OXIDAT?(3A)STAB?

FILE 'BIOTECHNO'
         43160 OXIDAT?
        108410 STAB?
           262 OXIDAT?(3A)STAB?
L82          0 L34 AND OXIDAT?(3A)STAB?

FILE 'WPIDS'
        130044 OXIDAT?
         62050 OXIDN
            89 OXIDNS
        158499 OXIDAT?
                 (OXIDAT? OR OXIDN OR OXIDNS)
        716228 STAB?
          6351 OXIDAT?(3A)STAB?
L83          4 L35 AND OXIDAT?(3A)STAB?

TOTAL FOR ALL FILES
L84          8 L36 AND OXIDAT?(3A) STAB?

=> s (124 or 148 or 160 or 172 or 184) not 2001-2004/py
FILE 'MEDLINE'
       1757359 2001-2004/PY
L85         40 (L13 OR L37 OR L49 OR L61 OR L73) NOT 2001-2004/PY

FILE 'SCISEARCH'
       3266666 2001-2004/PY
L86         48 (L14 OR L38 OR L50 OR L62 OR L74) NOT 2001-2004/PY

FILE 'LIFESCI'
        318557 2001-2004/PY
L87         23 (L15 OR L39 OR L51 OR L63 OR L75) NOT 2001-2004/PY

FILE 'BIOTECHDS'
         68344 2001-2004/PY
L88         37 (L16 OR L40 OR L52 OR L64 OR L76) NOT 2001-2004/PY

FILE 'BIOSIS'
       1737230 2001-2004/PY
```

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L89         45 (L17 OR L41 OR L53 OR L65 OR L77) NOT 2001-2004/PY

FILE 'EMBASE'
       1497643 2001-2004/PY
L90         34 (L18 OR L42 OR L54 OR L66 OR L78) NOT 2001-2004/PY

FILE 'HCAPLUS'
       3309953 2001-2004/PY
L91         77 (L19 OR L43 OR L55 OR L67 OR L79) NOT 2001-2004/PY

FILE 'NTIS'
         47098 2001-2004/PY
L92           1 (L20 OR L44 OR L56 OR L68 OR L80) NOT 2001-2004/PY

FILE 'ESBIOBASE'
        940850 2001-2004/PY
L93         21 (L21 OR L45 OR L57 OR L69 OR L81) NOT 2001-2004/PY

FILE 'BIOTECHNO'
        368875 2001-2004/PY
L94         25 (L22 OR L46 OR L58 OR L70 OR L82) NOT 2001-2004/PY

FILE 'WPIDS'
       3122570 2001-2004/PY
L95         17 (L23 OR L47 OR L59 OR L71 OR L83) NOT 2001-2004/PY

TOTAL FOR ALL FILES
L96        368 (L24 OR L48 OR L60 OR L72 OR L84) NOT 2001-2004/PY

=> fil .becpat
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                              ENTRY    SESSION
FULL ESTIMATED COST                           21.53      21.74

FILES 'BIOTECHDS, HCAPLUS, WPIDS' ENTERED AT 16:44:28 ON 20 APR 2004
ALL COPYRIGHTS AND RESTRICTIONS APPLY.  SEE HELP USAGETERMS FOR DETAILS.

3 FILES IN THE FILE LIST

=> s (l24 or l48 or l60 or l72 or l84) and wo/pc and pry<=2000 and py>=2001
range=2003,
FILE 'BIOTECHDS'
         10759 WO/PC
          3688 PRY<=2000
                 (PRY<=2000)
         36887 PY>=2001
                 (PY>=2001)
L97          0 (L16 OR L40 OR L52 OR L64 OR L76) AND WO/PC AND PRY<=2000 AND
               PY>=2001

FILE 'HCAPLUS'
         68456 WO/PC
         27087 PRY<=2000
       1314969 PY>=2001
L98          0 (L19 OR L43 OR L55 OR L67 OR L79) AND WO/PC AND PRY<=2000 AND
               PY>=2001

FILE 'WPIDS'
        151285 WO/PC
        140325 PRY<=2000
                 (PRY<=2000)
       1163697 PY>=2001
                 (PY>=2001)
L99          0 (L23 OR L47 OR L59 OR L71 OR L83) AND WO/PC AND PRY<=2000 AND
```

PY>=2001

TOTAL FOR ALL FILES
L100 0 (L24 OR L48 OR L60 OR L72 OR L84) AND WO/PC AND PRY<=2000 AND
PY>=2001

=> log y
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.55	29.29

STN INTERNATIONAL LOGOFF AT 16:45:57 ON 20 APR 2004

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	441	methionine adj aminopeptidase$	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:38
L2	7079	(methionine or met) same muta$10	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:38
L3	185	1 same 2	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:39
L4	1908	methionine same cysteine same muta$10	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:17
L5	102	4 same stab$8	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:18
L6	19342	oxidat$ near4 stab$8	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:25
L7	65	4 and 6	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:26
L8	2554	sulfur adj free	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:31
L10	1	8 near2 (protein$1 or enzyme$1)	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:32

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	441	methionine adj aminopeptidase$	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:38
L2	7079	(methionine or met) same muta$10	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:38
L3	185	1 same 2	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:39

PGPUB-DOCUMENT-NUMBER: 20040071700

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040071700 A1

TITLE: Obesity linked genes

PUBLICATION-DATE: April 15, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kim, Jaeseob	Yousong-Gu Taejon	WI	KR	
Galant, Ron	Madison		US	

APPL-NO: 10/ 267502

DATE FILED: October 9, 2002

US-CL-CURRENT: 424/145.1, 435/7.2

ABSTRACT:

The present invention relates to newly identified nucleic acids, their encoded proteins, and to the use of such nucleic acids and proteins. The invention also relates the correlation between the expression of genes and fat cell size and number. The invention also relates to modifying the activity of a protein that affects the number and/or size of fat cells by regulating the expression of the nucleic acids, homologs, or active variants or their encoded proteins.

---------- KWIC ---------

Detail Description Paragraph - DETX (112):

[0123] In addition, the present invention provides fragments of the polypeptides (i.e., truncation mutants). In some embodiments of the present invention, when expression of a portion of the protein is desired, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al., J. Bacteriol., 169:751 (1987)) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al., Proc. Natl. Acad. Sci. USA 84:2718 (1990)). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing such recombinant polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP.

PGPUB-DOCUMENT-NUMBER: 20040067535

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040067535 A1

TITLE: Alzheimer's disease linked genes

PUBLICATION-DATE: April 8, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kim, Jaeseob	Yousong-Gu Taejon	WI	KR	
Galant, Ron	Madison		US	

APPL-NO: 10/ 263929

DATE FILED: October 3, 2002

US-CL-CURRENT: 435/7.2, 800/12

ABSTRACT:

The present invention relates to newly identified nucleic acids, their encoded proteins, and to the use of such nucleic acids and proteins. The invention also relates the correlation between the expression of genes and Alzheimer's disease. The invention also relates to modifying the activity of a protein that affects Alzheimer's disease by regulating the expression of the nucleic acids, homologs, or active variants or their encoded proteins.

---------- KWIC ---------

Detail Description Paragraph - DETX (115):

[0136] In addition, the present invention provides fragments of the polypeptides (i.e., truncation mutants). In some embodiments of the present invention, when expression of a portion of the protein is desired, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al., J. Bacteriol. 169:751 (1987)) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al., Proc. Natl. Acad. Sci. USA 84:2718 (1990)). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing such recombinant polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP.

PGPUB-DOCUMENT-NUMBER: 20040043388

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040043388 A1

TITLE: Three hybrid assay system

PUBLICATION-DATE: March 4, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Come, Jon H.	Cambridge	MA	US	
Becker, Frank	Planegg	MA	DE	
Kley, Nikolai A.	Wellesley		US	
Reichel, Christoph	Planegg		DE	

APPL-NO: 10/ 234985

DATE FILED: September 3, 2002

RELATED-US-APPL-DATA:

child 10234985 A1 20020903

parent continuation-in-part-of 10091177 20020304 US PENDING

non-provisional-of-provisional 60272932 20010302 US

non-provisional-of-provisional 60278233 20010323 US

non-provisional-of-provisional 60329437 20011015 US

US-CL-CURRENT: 435/6, 435/7.1 , 530/317 , 530/350 , 536/123 , 536/23.1 , 540/200 , 546/1 , 552/200 , 552/500 , 552/653 , 556/118

ABSTRACT:

The invention provides compositions and methods for isolating ligand binding polypeptides for a user-specified ligand, and for isolating small molecule ligands for a user-specified target polypeptide using an improved class of hybrid ligand compounds.

REFERENCE TO RELATED APPLICATIONS

[0001] This application is a "continuation in part (CIP)" application of U.S. Ser. No. 10/091,177, filed on Mar. 4, 2002, which claims priority to U.S. Provisional applications No. 60/272,932, filed on Mar. 2, 2001; No. 60/278,233, filed on Mar. 23, 2001; and No. 60/329,437, filed on Oct. 15, 2001, the specifications of which are hereby incorporated by reference in their entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (310):
[0435] When it is desirable to express only a portion of a protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which

lacks the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its ire vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing polypeptides in a host which produces MAP (e.g., E. coli ox CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

PGPUB-DOCUMENT-NUMBER: 20040038202

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040038202 A1

TITLE: Epizootic catarrhal enteritis prevention, treatment and diagnosis

PUBLICATION-DATE: February 26, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Maes, Roger K.	Okemos	MI	US	
Wise, Annabel G.	Bath	MI	US	
Kiupel, Matti	Laingsburg	MI	US	

APPL-NO: 10/ 354606

DATE FILED: January 30, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60353608 20020131 US

US-CL-CURRENT: 435/5, 435/235.1 , 435/320.1 , 435/325 , 435/69.1 , 530/350 , 530/388.3 , 536/23.72

ABSTRACT:

The present invention relates to the use of novel nucleotide sequences for the spike peptide, pol region peptide and M and N region peptide of the ferret coronavirus and derivative products for the diagnosis and treatment of epizootic catarrhal enteritis (ECE) in ferrets.

---------- KWIC ---------

Detail Description Paragraph - DETX (161):

[0218] In addition, the present invention provides fragments of ferret coronavirus, M and N region peptide, pol peptide and spike peptide (i.e., truncation mutants, e.g., portions of SEQ ID NOS: 1, 4 and 12). In other embodiments, the present invention provides domains of ferret coronavirus, M and N region peptide, pol peptide and spike peptide (e.g., the binding domain). In some embodiments of the present invention, when expression of a portion of the ferret coronavirus, M and N region peptide, pol peptide and spike peptide is desired, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol., 169:751) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1990) Proc. Natl. Acad. Sci. USA 84:2718). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing such recombinant polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP.

PGPUB-DOCUMENT-NUMBER: 20040033607

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040033607 A1

TITLE: Plant vernalization independence (VIP) genes, proteins, and methods of use

PUBLICATION-DATE: February 19, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Van Nocker, Steven R.	East Lansing	MI	US	
Zhang, Hua	Holt	MI	US	

APPL-NO: 10/ 427224

DATE FILED: May 1, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60376765 20020501 US

US-CL-CURRENT: 435/468, 435/320.1 , 435/419 , 435/69.1 , 530/350 , 536/23.6 , 800/278

ABSTRACT:

The present invention relates to plant genes involved in regulating flowering, and especially to genes involved in the induction of flowering in response to cold, or vernalization. In particular, the present invention provides the identification, cloning, and characterization of genes involved in vernalization, and specifically of VIP genes, as well as to the proteins encoded by these genes, and to methods of using the VIP genes and proteins. Mutants of VIP genes, where the mutation is a knock-out mutation, confer a vernalization independence, or constitutively vernalized, phenotype in a plant which in the non-mutant form requires vernalization to flower.

[0001] The present application claims priority to U.S. patent application Ser. No. 60/376,765, filed May 1, 2002, which is hereby incorporated by reference in its entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (182):

[0215] e. Truncation Mutants of VIP. In addition, the present invention provides isolated nucleic acid sequences encoding fragments of encoded VIP products (i.e., truncation mutants), and the polypeptides encoded by such nucleic acid sequences. In preferred embodiments, the VIP fragment is biologically active. In some embodiments of the present invention, when expression of a portion of a VIP protein is desired, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme

methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al., J. Bacteriol., 169:751-757 [1987]) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al., Proc. Natl. Acad. Sci. USA, 84:2718-1722 [1990]). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing such recombinant polypeptides in a host that produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP.

PGPUB-DOCUMENT-NUMBER: 20040029118

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040029118 A1

TITLE: Streptococcus pneumoniae polynucleotides and sequences

PUBLICATION-DATE: February 12, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kunsch, Charles A.	Norcross	GA	US	
Choi, Gil H.	Rockville	MD	US	
Dillon, Patrick J.	Carlsbad	CA	US	
Rosen, Craig A.	Laytonsville	MD	US	
Barash, Steven C.	Rockville	MD	US	
Fannon, Michael R.	Silver Spring	MD	US	
Dougherty, Brian A.	Killingworth	CT	US	

APPL-NO: 10/ 158844

DATE FILED: June 3, 2002

RELATED-US-APPL-DATA:

child 10158844 A1 20020603

parent division-of 08961527 19971030 US GRANTED

parent-patent 6420135 US

non-provisional-of-provisional 60029960 19961031 US

US-CL-CURRENT: 435/6, 702/20

ABSTRACT:

The present invention provides polynucleotide sequences of the genome of Streptococcus pneumoniae, polypeptide sequences encoded by the polynucleotide sequences, corresponding polynucleotides and polypeptides, vectors and hosts comprising the polynucleotides, and assays and other uses thereof. The present invention further provides polynucleotide and polypeptide sequence information stored on computer readable media, and computer-based systems and methods which facilitate its use.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application is a divisional of and claims priority under 35 U.S.C. .sctn.120 to U.S. application Ser. No. 08/961,527, filed Oct. 30, 1997, which is a nonprovisional of and claims benefit under 35 U.S.C. .sctn.119(e) of U.S. Provisional Application No. 60/029,960, filed Oct. 31, 1996.

---------- KWIC ---------

Detail Description Table CWU - DETL (19):
76 5 5773 4097 gnl.vertline.PID.vertline.d101723 DNA REPAIR PROTEIN RECN

65 44 1677 (RECOMBINATION PROTEIN N). [Escherichia coli] 76 9 8099 7875
gi.vertline.1574276 exodeoxyribonuclease, small subunit 65 38 225 (xseB)
[Haemophilus influenzae] 84 2 2870 2352 gi.vertline.2313188 (AE000532)
conserved hypothetical 65 41 519 protein [Helicobacter pylori] 86 15 14495
13407 gnl.vertline.PID.vertline.- d101880 3-dehydroquinate synthase [65 44
1089 Synechocystis sp.] 87 3 3706 2423 gi.vertline.151259 HMG-CoA reductase
(EC 1.1.1.88) 65 51 1284 [Pseudomonas mevalonii] 88 3 2425 2736
gi.vertline.1098510 unknown [Lactococcus lactis] 65 30 312 89 2 1627 1007
gnl.vertline.PID.vertline.d102008 (AB001488) SIMILAR TO ORF14 OF 65 41 621
ENTEROCOCCUS FAECALIS TRANSPOSON TN916. [Bacillus subtilis] 111 6 6635 6186
gnl.vertline.PID.vertli- ne.e246063 NM23/nucleoside diphosphate kinase 65 50
450 [Xenopus laevis] 116 1 3 1016 gnl.vertline.PID.vertline.d101125
queuosine biosynthesis protein QueA 65 44 1014 [Synechocystis sp.] 123 1 69
389 gi.vertline.498839 ORF2 [Clostridium perfringens] 65 36 321 123 7 6522
7190 gi.vertline.1575577 DNA-binding response regulator [Thermotoga maritima]
65 39 669 125 3 3821 2859 gnl.vertline.PID.vertline.e257609 sugar-binding
transport protein 65 47 963 [Anaerocellum thermophilum] 137 12 8015 7818
gi.vertline.2182574 (AE000090) Y4pE [Rhizobium sp. NGR234] 65 41 198 147 4
5021 3885 gi.vertline.472329 dihydrolipoamide acetyltransferase 65 47 1137
[Clostridium magnum] 148 2 1053 1931 gnl.vertline.PID.vertline.d101319 YqgH
[Bacillus subtilis] 65 42 879 151 2 3212 4687 gi.vertline.304897 EcoE type I
restriction modification 65 50 1476 enzyme M subunit [Escherichia coli] 156
2 730 437 gi.vertline.310893 membrane protein [Theileria parva] 65 47 294 164
7 4256 4837 gi.vertline.410132 ORFX8 [Bacillus subtilis] 65 48 582 169 6 3192
3914 gi.vertline.1552737 similar to purine nucleoside 65 41 723 phosphorylase
(deoD) [Escherichia coli] 176 4 2951 2220 gnl.vertline.PID.vertline.e3395-
00 oligopeptide binding lipoprotein 65 43 732 [Streptococcus pneumoniae] 195
4 4556 3900 gi.vertline.1592142 ABC transporter, probable 65 40 657
ATP-binding subunit [Methanococcus jannaschii] 196 1 160 1572
gnl.vertline.PID.vertlin- e.d102004 (AB001488) PROBABLE UDP-N-ACETYL- 65 51
1413 MURAMOYLALANYL-D-GLUTAMYL- 2, 6-DIAMINOLIGASE (EC 6.3.2.15). [Bacillus
subtilis] 204 2 2246 1215 gi.vertline.143156 membrane bound protein 65 37
1032 [Bacillus subtilis] 210 4 1544 1891 gi.vertline.49315 ORF1 gene product
65 48 348 [Bacillus subtilis] 242 2 1625 723 gi.vertline.1787540 (AE000226)
f249; This 249 aa orf is 32 65 42 903 pct identical (8 gaps) to 244 residues
of an approx. 272 aa protein AGAR_ECOLI SW P42902 [Escherichia coli] 284 1 1
900 gi.vertline.559861 clyM [Plasmid pAd1] 65 36 900 304 1 2 574
gnl.vertline.PID.vertlin- e.e290934 unknown [Mycobacterium tuberculosis] 65 52
573 315 1 2 1483 gi.vertline.790694 mannuronan C-5-epimerase 65 57 1482
[Azotobacter vinelandii] 320 1 3 569 gnl.vertline.PID.vertline.d10- 2048 K.
aerogenes, histidine utilization 65 46 567 repressor; P12380 (199) DNA
binding [Bacillus subtilis] 358 1 1 309 gnl.vertline.PID.vertline.e323508
YloS protein [Bacillus subtilis] 65 55 309 2 7 7571 6696 gi.vertline.1498753
nicotinate-nucleotide pyrophosphorylase 64 47 876 [Rhodospirillum rubrum] 6
6 5924 6802 gnl.vertline.PID.vertline.d101111 methionine aminopeptidase 64 52
879 [Synechocystis sp.] 8 4 3417 3686 gi.vertline.1045935 DNA helicase II
[Mycoplasma genitalium] 64 58 270 11 4 3249 2689
gnl.vertline.PID.vertline.e265529 OrfB [Streptococcus pneumoniae] 64 46 561
15 7 6504 7145 gi.vertline.1762328 Ycr59c/YigZ homolog [Bacillus subtilis] 64
45 642 22 11 9548 9895 gnl.vertline.PID.vertline.d100581 unknown [Bacillus
subtilis] 64 38 348 22 30 22503 23174 gi.vertline.289260 comE ORF1 [Bacillus
subtilis] 64 44 672 26 7 14375 14199 gi.vertline.409286 bmrU [Bacillus
subtilis] 64 30 177 27 2 1510 1334 gi.vertline.40795 DdeI methylase
[Desulfovibrio vulgaris] 64 51 177 29 2 614 297 gi.vertline.2326168 type VII
collagen [Mus Musculus] 64 50 318 35 2 368 721
pir.vertline.JC1151.vertline.JC11 hypothetical 20.3K protein 64 50 354
(insertion sequence IS1131) - Agrobacterium tumefaciens (strain PO22) plasmid
Ti 40 1 3 449 gi.vertline.46970 epiD gene product 64 41 447 [Staphylococcus
epidermidis] 40 7 4683 4976 gnl.vertline.PID.vertline.e325792 (AJ000005)

glucose kinase 64 45 294 [Bacillus megaterium] 45 7 8068 6920 gnl.vertline.PID.vertline.d102036 subunit of ADP-glucose 64 40 1149 pyrophosphorylase [Bacillus stearothermophilus] 51 2 301 1059 gi.vertline.43985 nifs-like gene [Lactobacillus 64 54 759 delbrueckii] 51 13 15251 18397 gi.vertline.2293260 (AF008220) DNA-polymerase III 64 46 3147 alpha-chain [Bacillus subtilis] 53 3 1157 555 gi.vertline.1574292 hypothetical [Haemophilus 64 47 603 influenzae] 58 2 4236 1606 gi.vertline.1573826 alanyl-tRNA synthetase (alaS) 64 51 2631 [Haemophilus influenzae] 66 1 3 1259 gi.vertline.895749 putative cellobiose phospho- 64 42 1257 transferase enzyme II" [Bacillus subtilis] 68 5 5213 6556 gi.vertline.436965 [malA].sup.-gene products 64 47 1344 [Bacillus stearothermophilus] 69 6 5356 4949 gnl.vertline.PID.vertline.d1013- 16 Cdd [Bacillus subtilis] 64 52 408 74 4 6948 5038 gi.vertline.726480 L-glutamine-D-fructose-6-phosphate 64 50 1911 amidotransferase [Bacillus subtilis] 75 3 1283 1465 bbs.vertline.133379 TLS-CHOP = fusion protein 64 57 183 (CHOP = C/EBP transcription factor, TLS = nuclear RNA-binding protein) [human, myxoid liposarcomas cells, Peptide Mutant, 462 aa] [Homo sapiens] 81 13 14016 14231 gi.vertline.143175 methanol dehydrogenase alpha-10 subunit 64 35 216 [Bacillus sp.] 83 22 21851 22090 gnl.vertline.PID.vertline.-d101315 YqfA [Bacillus subtilis] 64 44 240 87 11 10046 9300 gnl.vertline.PID.vertline.e323505 putative Ptc1 protein [Bacillus 64 43 747 subtilis] 98 7 5032 5706 gnl.vertline.PID.vertline- .e233880 hypothetical protein [Bacillus 64 38 675 subtilis] 105 1 2 1276 gi.vertline.1657503 similar to S. aureus mercury (II) 64 45 1275 reductase [Escherichia coli] 113 7 5136 6410 gnl.vertline.PID.vertline.d101119 NifS [Synechocystis sp.] 64 50 1275 119 1 2 1297 gnl.vertline.PID.vertline.e320520 hypothetical protein 64 37 1296 [Natronobacterium pharaonis] 123 3 1125 2156 gnl.vertline.PID.vertline.e253284 ORF YDL244w [Saccharomyces 64 40 1032 cerevisiae] 124 5 2331 1780 gnl.vertline.PID.vertline.d1- 01884 hypothetical protein [Synechocystis sp.] 64 50 552 129 4 3467 2709 gnl.vertline.PID.vertline.d101314 YqeU [Bacillus subtilis] 64 52 759 131 1 152 3 gi.vertline.1377841 unknown [Bacillus subtilis] 64 42 150 137 11 7196 7549 pir.vertline.JC1151.vertline.JC11 hypothetical 20.3K protein 64 50 354 (insertion sequence IS1131) - Agrobacterium tumefaciens (strain PO22) plasmid Ti 139 3 3226 2651 gi.vertline.2293301 (AF008220) YtqB [Bacillus subtilis] 64 44 576 146 10 6730 5648 gi.vertline.1322245 mevalonate pyrophosphate decar- 64 45 1083 boxylase [Rattus norvegicus] 147 1 2 1018 gnl.vertline.PID.vertline.e137033 unknown gene product 64 46 1017 [Lactobacillus leichmannii] 148 11 8430 8783 gi.vertline.2130630 (AF000430) dynamin-like protein 64 28 354 [Homo sapiens] 156 7 4313 3612 gnl.vertline.PID.vertline.d102050 transmembrane [Bacillus subtilis] 64 31 702 157 4 1299 2114 gnl.vertline.PID.vertline.d100892 homologous to Gln transport 64 43 816 system permease proteins [Bacillus subtilis] 162 6 5880 6362 gi.vertline.517204 ORF1, putative 42 kDa protein 64 58 483 [Streptococcus pyogenes] 164 13 9707 8769 gnl.vertline.PID.vertline.d100964 homologue of ferric anguibactin 64 40 939 transport system permerase protein FatD of V. anguillarum [Bacillus subtilis] 175 5 3906 4598 gi.vertline.534045 antiterminator [Bacillus subtilis] 64 39 693 189 10 6154 6507 gi.vertline.581307 response regulator [Lactobacillus 64 33 354 plantarum] 191 4 3519 2863 gi.vertline.149520 phosphoribosyl anthranilate iso- 64 46 657 merase [Lactococcus lactis] 202 1 76 1140 gnl.vertline.PID.vertlin- e.e293806 O-acetylhomoserine sulfhydrylase 64 47 1065 [Leptospira meyeri] 224 1 234 1571 gi.vertline.1573393 collagenase (prtC) [Haemophilius 64 42 1338 influenzae] 231 3 291 647 gi.vertline.40174 ORF X [Bacillus subtilis] 64 43 357

PGPUB-DOCUMENT-NUMBER: 20040023234

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040023234 A1

TITLE: BSND nucleic acids and proteins

PUBLICATION-DATE: February 5, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hildebrandt, Friedhelm	Ann Arbor	MI	US	
Jentsch, Thomas J.	Hamburg		DE	

APPL-NO: 10/ 273476

DATE FILED: October 18, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60333637 20011126 US

non-provisional-of-provisional 60345002 20011019 US

US-CL-CURRENT: 435/6, 536/23.2

ABSTRACT:

The present invention relates to the BSND (barttin) protein and nucleic acids encoding the BSND protein. The present invention provides assays for the detection of BSND and barttin polymorphisms and mutations associated with disease states.

[0001] This application claims priority to U.S. provisional patent application filed on Oct. 19, 2001 with Express Mail Label ET720704983US and U.S. provisional patent application serial No. 60/333,637, filed Nov. 26, 2001.

---------- KWIC ---------

Detail Description Paragraph - DETX (115):

[0142] In addition, the present invention provides fragments of BSND (i.e., truncation mutants). In some embodiments of the present invention, when expression of a portion of the BSND protein is desired, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al., J. Bacteriol., 169:751 [1987]) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al., Proc. Natl. Acad. Sci. USA 84:2718 [1990]). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing such recombinant polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerivisiae), or in vitro by use of purified MAP.

PGPUB-DOCUMENT-NUMBER: 20040014209

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040014209 A1

TITLE: Compositions and methods for modulating cell differentiation

PUBLICATION-DATE: January 22, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lassar, Andrew B.	Newton Center	MA	US	
Mercola, Mark	Del Mar	CA	US	
Gupta, Ruchika	San Diego	CA	US	
Marvin, Martha	Brookline	MA	US	
Schneider, Valerie	Philadelphia	PA	US	
Tzahor, Eldad	Brookline	MA	US	
Brott, Barbara	Boston	MA	US	
Sokol, Sergei	Boston	MA	US	

APPL-NO: 10/ 351275

DATE FILED: January 23, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60351126 20020123 US

non-provisional-of-provisional 60352456 20020128 US

non-provisional-of-provisional 60352665 20020129 US

US-CL-CURRENT: 435/366, 435/455

ABSTRACT:

The present invention relates to compositions and methods for stimulating differentiation of stem cells into cardiac cells. The methods of the invention involve contacting a population cells comprising stem cells with at least one Wnt antagonist, such as a polypeptide or polypeptide fragment. In certain embodiments, the methods of the invention involve Dkk proteins or fragments, homologs, derivatives, variants, or peptidomimetics thereof.

RELATED APPLICATION INFORMATION

[0001] This application claims the benefit of priority to Provisional Patent Application Nos. 60/351,126, filed Jan. 23, 2002, 60/352,456, filed Jan. 28, 2002, and 60/352,665, filed Jan. 29, 2002, which applications are hereby incorporated by reference in their entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (81):
[0119] When expression of a carboxy terminal fragment of a polypeptide is desired, i.e. a truncation mutant, it may be necessary to add a start codon

(ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position may be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al., (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al., (1987) PNAS USA 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, may be achieved either in vivo by expressing such recombinant polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al.).

PGPUB-DOCUMENT-NUMBER: 20040010817

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040010817 A1

TITLE: Plant acyl-CoA synthetases

PUBLICATION-DATE: January 15, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Shockey, Jay M.	Mandeville	LA	US	
Schnurr, Judy	Coon Rapids	MN	US	
Browse, John A.	Palouse	WA	US	

APPL-NO: 10/ 410031

DATE FILED: April 9, 2003

RELATED-US-APPL-DATA:

child 10410031 A1 20030409

parent continuation-in-part-of 10119136 20020409 US PENDING

child 10119136 20020409 US

parent continuation-in-part-of 09906419 20010716 US ABANDONED

non-provisional-of-provisional 60220474 20000721 US

US-CL-CURRENT: 800/281, 435/193 , 435/320.1 , 435/419 , 435/69.1 , 536/23.2

ABSTRACT:

The present invention relates to genes encoding plant acyl-CoA synthetases and methods of their use. In particular, the present invention is related to plant acyl-coenzyme A synthetases. The present invention encompasses both native and recombinant wild-type forms of the enzymes, as well as mutant and variant forms, some of which possess altered characteristics relative to the wild-type enzyme. The present invention also relates to methods of using acyl-CoA synthetases, including altered expression in transgenic plants and expression in prokaryotes and cell culture systems.

[0001] This is a Continuation-In-Part of copending application Ser. No. 10/119,136 filed on Mar. 9, 2002, which is a Continuation-In-Part of copending Ser. No. 09/906,419 filed on Jul. 16, 2001, which claimed priority from provisional application 60/220,474 filed on Jul. 21, 2000, now abandoned.

---------- KWIC ---------

Detail Description Paragraph - DETX (168):
[0289] The present invention further provides fragments of ACSs. In some embodiments of the present invention, when expression of a portion of an ACS is

desired, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and S. typhimurium, and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1990) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing such recombinant polypeptides in a host producing MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP. It is contemplated that deletion mutants of ACSs can be screened for activity as described above.

PGPUB-DOCUMENT-NUMBER: 20040009154

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040009154 A1

TITLE: Selections of genes and methods of using the same for diagnosis and for targeting the therapy of select cancers

PUBLICATION-DATE: January 15, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Khan, Javed	Derwood	MD	US	
Ringner, Markus	Lund	MD	SE	
Peterson, Carsten	Lund		SE	
Meltzer, Paul	Rockville		US	

APPL-NO: 10/ 159563

DATE FILED: May 31, 2002

RELATED-US-APPL-DATA:

child 10159563 A1 20020531

parent continuation-in-part-of 10133937 20020425 US PENDING

US-CL-CURRENT: 424/93.21, 514/44 , 536/23.2

ABSTRACT:

A method of diagnosing a disease that includes obtaining experimental data on gene selections. The gene selection functions to characterize a cancer when the expression of that gene selection is compared to the identical selection from a noncancerous cell or a different type of cancer cell. The invention also includes a method of targeting at least one product of a gene that includes administration of a therapeutic agent. The invention also includes the use of a gene selection for diagnosing a cancer.

[0001] This application is a continuation in part of a U.S. patent application Ser. No. 10/133,937 entitled "METHODS FOR ANALYZING HIGH DIMENSIONAL DATA FOR CLASSIFYING, DIAGNOSING, PROGNOSTICATING, AND/OR PREDICTING DISEASES AND OTHER BIOLOGICAL STATES", filed on Apr. 25, 2002.

---------- KWIC ---------

Detail Description Table CWU - DETL (9):
9TABLE 5 Unique Unigene Rank Image_Id Name of Gene number Weight 1 296448 "insulin-like growth factor 2 Hs.251664 1.00 + -0.03 (somatomedin A)" 2 207274 "insulin-like growth factor 2 Hs.251664 0.97 + -0.03 (somatomedin A)" 3 295985 "Homo sapiens cDNA FLJ20653 fis, Hs.180059 0.87 + -0.02 clone KAT01739" 4 41591 "meningioma (disrupted in balanced Hs.268515 0.86 + -0.02 translocation) 1" 5 365826 "growth arrest-specific 1" Hs.65029 0.86 + -0.02

6 714453 "interleukin 4 receptor" Hs.75545 0.85 + -0.02 7 812965 "v-myc avian myelocytomatosis viral Hs.79070 0.81 + -0.02 oncogene homolog" 8 486787 "calponin 3, acidic" Hs.194662 0.81 + -0.02 9 244618 "ESTs" Hs.15463 0.80 + -0.02 10 417226 "v-myc avian myelocytomatosis viral Hs.79070 0.80 + -0.02 oncogene homolog" 11 840942 "major histocompatibility complex, Hs.814 0.79 + -0.02 class II, DP beta 1" 12 770394 "Fc fragment of IgG, receptor, Hs.160741 0.78 + -0.02 transporter, alpha" 13 812105 "ALL1-fused gene from chromosome Hs.75823 0.76 + -0.02 1q" 14 357031 "tumor necrosis factor, alpha-induced Hs.29352 0.75 + -0.02 protein 6" 15 629896 "microtubule-associated protein 1B" Hs.103042 0.74 + -0.02 16 308163 "ESTs" Hs.84520 0.73 + -0.02 17 43733 "glycogenin 2" Hs.58589 0.72 + -0.02 18 489631 "chondroitin sulfate proteoglycan 2 Hs.81800 0.71 + -0.02 (versican)" 19 866702 "protein tyrosine phosphatase, non- Hs.211595 0.71 + -0.02 receptor type 13 (APO-1/CD95 (Fas)- associated phosphatase)" 20 377461 "caveolin 1, caveolae protein, 22 kD" Hs.281621 0.70 + -0.02 21 324494 "heat shock 27 kD protein 2" Hs.78846 0.69 + -0.02 22 80109 "major histocompatibility complex, Hs.198253 0.69 + -0.02 class II, DQ alpha 1" 23 39093 "methionine aminopeptidase; eIF-2- Hs.78935 0.69 + -0.01 associated p67" 24 82225 "secreted frizzled-related protein 1" Hs.7306 0.67 + -0.01 25 308231 "Homo sapiens cDNA FLJ20153 fis, Hs.109805 0.67 + -0.02 clone COL08656, highly similar to AJ001381 Homo sapiens incomplete cDNA for a mutated allele" 26 211758 "ribosomal protein S23" Hs.3463 0.67 + -0.01 27 1E+06 "troponin T1, skeletal, slow" Hs.73980 0.66 + -0.02 28 878280 "collapsin response mediator protein 1" Hs.155392 0.65 + -0.02 29 383188 "recoverin" Hs.80539 0.64 + -0.01 30 795877 "serum-inducible kinase" Hs.3838 0.64 + -0.01 31 784593 "ESTs" Hs.6838 0.63 + -0.01 32 135688 "GATA-binding protein 2" Hs.760 0.62 + -0.01 33 325182 "cadherin 2, N-cadherin (neuronal)" Hs.161 0.62 + -0.01 34 461425 "myosin, light polypeptide 4, alkali; Hs.154156 0.61 + -0.01 atrial, embryonic" 35 1E+06 "transducin-like enhancer of split 2, Hs.173063 0.61 + -0.02 homolog of Drosophila E(sp1)" 36 298062 "troponin T2, cardiac" Hs.89749 0.61 + -0.02 37 841641 "cyclin D1 (PRAD1: parathyroid Hs.82932 0.61 + -0.01 adenomatosis 1)" 38 745343 "regenerating islet-derived 1 alpha Hs.1032 0.60 + -0.01 (pancreatic stone protein, pancreatic thread protein)" 39 755599 "interferon induced transmembrane Hs.146360 0.59 + -0.02 protein 1 (9-27)" 40 809901 "collagen, type XV, alpha 1" Hs.83164 0.59 + -0.01 41 859359 "quinone oxidoreductase homolog" Hs.50649 0.59 + -0.01 42 784224 "fibroblast growth factor receptor 4" Hs.165950 0.59 + -0.02 43 42558 "glycine amidinotransferase (L- Hs.75335 0.58 + -0.01 arginine: glycine amidinotransferase)" 44 183337 "major histocompatibility complex, Hs.77522 0.58 + -0.01 class II, DM alpha" 45 289645 "amyloid beta (A4) precursor-like Hs.74565 0.58 + -0.01 protein 1" 46 377048 "Homo sapiens cDNA FLJ20153 fis, Hs.109805 0.57 + -0.01 clone COL08656, highly similar to AJ001381 Homo sapiens incomplete cDNA for a mutated allele" 47 122159 "collagen, type III, alpha 1 (Ehlers- Hs.119571 0.57 + -0.01 Danlos syndrome type IV, autosomal dominant)" 48 245330 "insulin-like growth factor 2 Hs.251664 0.57 + -0.01 (somatomedin A)" 49 814260 "follicular lymphoma variant Hs.74050 0.57 + -0.01 translocation 1" 50 824602 "interferon, gamma-inducible protein Hs.155530 0.57 + -0.01 16" 51 44563 "growth associated protein 43" Hs.79000 0.56 + -0.01 52 767495 "GLI-Kruppel family member GLI3 Hs.72916 0.56 + -0.01 (Greig cephalopolysyndactyly syndrome)" 53 769716 "neurofibromin 2 (bilateral acoustic Hs.902 0.55 + -0.01 neuroma)" 54 486110 "profilin 2" Hs.91747 0.55 + -0.01 55 1E+06 "pim-2 oncogene" Hs.80205 0.55 + -0.01 56 756556 "complement component 1 inhibitor Hs.151242 0.54 + -0.01 (angioedema, hereditary)" 57 377731 "glutathione S-transferase M5" Hs.75652 0.54 + -0.01 58 52076 "olfactomedin related ER localized Hs.74376 0.54 + -0.02 protein" 59 810057 "cold shock domain protein A" Hs.1139 0.54 + -0.01 60 233721 "insulin-like growth factor binding Hs.162 0.54 + -0.01 protein 2 (36 kD)" 61 293500 "ESTs" Hs.49714 0.54 + -0.01 62 75254 "cysteine and glycine-rich protein 2 Hs.10526 0.54 + -0.01 (LIM domain only, smooth muscle)" 63 377468 "sprouty

(Drosophila) homolog 1 Hs.88044 0.53 + -0.01 (antagonist of FGF signaling)" 64 809910 "interferon induced transmembrane Hs.182241 0.53 + -0.01 protein 3 (1-8U)" 65 395708 "dihydropyrimidinase-like 4" Hs.100058 0.53 + -0.01 66 416959 "nuclear factor I/B" Hs.33287 0.53 + -0.01 67 1E+06 "antigen identified by monoclonal Hs.177543 0.52 + -0.01 antibodies 12E7, F21 and O13" 68 609663 "protein kinase, cAMP-dependent, Hs.77439 0.51 + -0.01 regulatory, type II, beta" 69 212640 "Rho GTPase activating protein 4" Hs.3109 0.51 + -0.01 70 130057 "ESTs" Hs.23057 0.51 + -0.01 71 563673 "antiquitin 1" Hs.74294 0.51 + -0.01 72 770059 "heparan sulfate proteoglycan 2 Hs.211573 0.51 + -0.01 (perlecan)" 73 782503 "Homo sapiens clone 23716 mRNA Hs.12214 0.50 + -0.01 sequence" 74 292522 "ESTs" Hs.38022 0.50 + -0.01 75 365515 "fibroblast growth factor 7 (keratinocyte Hs.164568 0.50 + -0.01 growth factor)" 76 1E+06 "cysteine-rich protein 1 (intestinal)" Hs.17409 0.50 + -0.01 77 767183 "hematopoietic cell-specific Lyn Hs.14601 0.50 + -0.01 substrate 1" 78 811000 "lectin, galactoside-binding, soluble, 3 Hs.79339 0.50 + -0.01 binding protein (galectin 6 binding protein)" 79 308497 "KIAA0467 protein" Hs.11147 0.49 + -0.01 80 80338 "selenium binding protein 1" Hs.7833 0.49 + -0.01 81 200814 "membrane metallo-endopeptidase Hs.1298 0.49 + -0.01 (neutral endopeptidase, enkephalinase, CALLA, CD10)" 82 898219 "mesoderm specific transcript (mouse) Hs.79284 0.49 + -0.01 homolog" 83 796258 "sarcoglycan, alpha (50 kD dystrophin- Hs.99931 0.49 + -0.01 associated glycoprotein)" 84 377671 "integrin, alpha 7" Hs.74369 0.48 + -0.01 85 839736 "crystallin, alpha B" Hs.1940 0.48 + -0.01 86 208718 "annexin A1" Hs.78225 0.48 + -0.01 87 32299 "inositol(myo)-1(or 4)- Hs.5753 0.48 + -0.01 monophosphatase 2" 88 246377 "EST" Hs.102670 0.48 + -0.01 89 413633 "EST" -- 0.48 + -0.01 90 140806 "peptidylglycine alpha-amidating Hs.83920 0.47 + -0.01 monooxygenase" 91 294496 "ESTs" Hs.23037 0.47 + -0.01 92 755750 "non-metastatic cells 2, protein Hs.275163 0.47 + -0.01 (NM23B) expressed in" 93 811108 "thyroid hormone receptor interactor 6" Hs.119498 0.47 + -0.01 94 246035 "ESTs" Hs.78026 0.47 + -0.01 95 796904 "pleomorphic adenoma gene-like 1" Hs.75825 0.47 + -0.01 96 788107 "bridging integrator 1" Hs.193163 0.47 + -0.01 97 714106 "plasminogen activator,

PGPUB-DOCUMENT-NUMBER: 20040005644

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040005644 A1

TITLE: Method and composition for detection and treatment of breast cancer

PUBLICATION-DATE: January 8, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Su, Yan A.	Bethesda	MD	US	
Yang, Jun	Hinsdale	IL	US	

APPL-NO: 10/ 373801

DATE FILED: February 27, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60359999 20020228 US

US-CL-CURRENT: 435/7.23

ABSTRACT:

The present invention provides a method for the detection of breast cancer using breast by measuring expression levels of breast cancer specific marker (BCSM) genes, and in particular the level of polynucleotides transcribed from and polypeptides encoded by the BCSM genes. The present invention also provide a method for the treatment and/or prevention of breast cancer by modulating the activity of BCSM genes or the products of BCSM genes.

RELATED APPLICATION

[0001] This application is related to U.S. Provisional Application Serial No. 60/359,999, filed Feb. 28, 2002.

---------- KWIC ---------

Detail Description Table CWU - DETL (2):
784278 SF100 nuclear antigen Sp100 LCC2c9 784841 EIF2S3 eukaryotic translation initiation factor 2, subunit 3 (gamma, 52 kD) LCC2b10 786048 E2F4 E2F transcription factor 4, p107/p130-binding LCC3a3 788574 GCN5L2 GCN5 (general control of amino-acid synthesis, yeast, homolog)-like 2 LCC2g8 789232 PSMD4 proteasome (prosome, macropain) 26S subunit, non-ATPase, 4 LCC2g4 795282 HSPC126 HSPC126 protein LCC4h3 795330 NR1D1 nuclear receptor subfamily 1, group D, member 1 LCC2b11 795888 RBBP2 retinoblastoma-binding protein 2 LCC2b12 809517 PRO2605 hypothetical protein PRO2605 LCC4g7 809648 ZNF162 zinc finger protein 162 LCC2g10 809835 HNRPC heterogeneous nuclear ribonucleoprotein C (C1/C2) LCC8d12 809992 PSMD2 proteasome (prosome, macropain) 26S subunit, non-ATPase, 2 LCC1g9 809992 PSMD2 proteasome (prosome, macropain) 26S subunit, non-ATPase, 2 LCC8b8 810019 HNRPD heterogeneous nuclear ribonucleoprotein D (AU-rich element RNA-binding protein 1, 37 kD) LCC8a10 810791 MNAT1 menage a trois 1 (CAK assembly factor) LCC8b7

810873 SCNN1A sodium channel, nonvoltage-gated 1 alpha LCC1a8 811792 GSS glutathione synthetase LCC1h2 813158 DRG2 developmentally regulated GTP-binding protein 2 LCC1g11 813280 ADSL adenylosuccinate lyase LCC2a12 813426 G53955 GS3955 protein LCC1f4 813648 DLD dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, LCC8b10 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex) 813742 PTK7 PTK7 protein tyrosine kinase 7 LCC1b2 814508 PPP1R7 protein phosphatase 1, regulatory subunit 7 LCC2h9 814595 PRKCBP1 protein kinase C binding protein 1 LCC2d5 814636 SMARCA2 SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, LCC2e3 member 2 815542 MX1 myxovirus (influenza) resistance 1, homolog of marine (interferon-inducible protein p78) LCC2c10 815575 ACTR1A ARP1 (actin-related protein 1, yeast) homolog A (centractin alpha) LCC8f3 823930 ARPC1A actin related protein 2/3 complex, subunit 1A (41 kD) LCC1g7 824024 NQO2 NAD(P)H menadione oxidoreductase 2, dioxin-inducible LCC2c3 824031 HSJ2 heat shock protein, DNAJ-like 2 LCC3a7 824602 IFI16 interferon, gamma-inducible protein 16 LCC2f7 825470 TOP2A topoisomerase (DNA) II alpha (170 kD) LCC2b7 838366 HMGCL 3-hydroxymethyl-3-methylglutaryl-Coenzyme A lyase (hydroxymethylglutaricaciduria) LCC8g4 840404 MGAT2 mannosyl (alpha-1,6-)-glycoprotein beta-1,2-N-acetylglucosaminyltransferase LCC2g6 840940 PABPC1 poly(A)-binding protein, cytoplasmic 1 LCC2c8 841691 MNPEP methionine aminopeptidase; eIF-2-associated p67 LCC8c9 843016 P130 nucleolar phosphoprotein p130 LCC2f5 843328 DUSP12 dual specificity phosphatase 12 LCC5c2 852520 UQCRC2 ubiquinol-cytochrome c reductase core protein II LCC8e2 853570 SLC25A6 solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 6 LCC8f5 855910 LGALS3 lectin, galactoside-binding, soluble, 3 (galectin 3) LCC5a9 866882 FDFT1 farnesyl-diphosphate farnesyltransferase 1 LCC8e8 868368 TMSB4X thymosin, beta 4, X chromosome LCC5a11 877613 DCTN1 dynactin 1 (p150, Glued (Drosophila) homolog) LCC2h8 877832 DXS1357E accessory proteins BAP31/BAP29 LCC8e5 878545 RPL18 ribosomal protein L18 LCC6c9 884644 HBG1 hemoglobin, gamma A LCC5a10 897164 CTNNA1 catenin (cadherin-associated protein), alpha 1 (102 kD) LCC8e7 897177 PGAM1 phosphoglycerate mutase 1 (brain) LCC8e3 897626 PRO2706 hypothetical protein PRO2706 LCC2h11 897880 CCT4 chaperonin containing TCP1, subunit 4 (delta) LCC8d6 897983 KIAA0106 anti-oxidant protein 2 (non-selenium glutathione peroxidase, acidic calcium-independent LCC2f9 phospholipase A2) 898262 UBE1 ubiquitin-activating enzyme E1 (A1S9T and BN75 temperature sensitivity complementing) LCC8c3 949928 ZNF220 zinc finger protein 220 LCC2e2 950489 SOD1 superoxide dismutase 1, soluble (amyotrophic lateral sclerosis 1 (adult)) LCC8b12 950682 PFKP phosphofructokinase, platelet LCC8c5 951117 SHMT2 serine hydroxymethyltransferase 2 (mitochondrial) LCC3b6 951313 GP1 glucose phosphate isomerase LCC5c6 969854 CALM3 calmodulin 3 (phosphorylase kinase, delta) LCC8e4 971367 RPS8 ribosomal protein S8 LCC6c10 1160558 PTS 6-pyruvoyltetrahydropterin synthase LCC6c3 1340595 HNRPL heterogeneous nuclear ribonucleoprotein L LCC6b12 1416782 CKB creatine kinase, brain LCC8f7 1473300 HADHA hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A LCC8f11 hydratase (trifunctional protein), alpha subunit 1475028 RPS27 ribosomal protein S27 (metallopanstimulin 1) LCC6c8 1475730 CCT6A chaperonin containing TCP1, subunit 6A (zeta 1) LCC8f12

PGPUB-DOCUMENT-NUMBER: 20040002144

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040002144 A1

TITLE: Method for modifying transglutaminases from microorganisms

PUBLICATION-DATE: January 1, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kashiwagi, Tatsuki	Kawasaki-shi		JP	
Shimba, Nobuhisa	Kawasaki-shi		JP	
Ishikawa, Kohki	Kawasaki-shi		JP	
Suzuki, Ei-Ichiro	Kawasaki-shi		JP	
Yokoyama, Keiichi	Kawasaki-shi		JP	
Hirayama, Kazuo	Kawasaki-shi		JP	

APPL-NO: 10/ 365434

DATE FILED: February 13, 2003

RELATED-US-APPL-DATA:

child 10365434 A1 20030213

parent continuation-of PCT/JP01/07038 20010815 US UNKNOWN

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
JP	2000-247664	2000JP-2000-247664	August 17, 2000
JP	2000-396695	2000JP-2000-396695	December 27, 2000

US-CL-CURRENT: 435/193, 435/252.3 , 435/320.1 , 435/69.1 , 702/19

ABSTRACT:

The present invention relates to a method for designing and preparing mutant transglutaminases on the basis of the three-dimensional structure of MTG derived from Streptoverticillium mobaraense (MTG), and the mutant MTG thus prepared. The present invention provides a method for modifying MTG on the basis of the three-dimensional structure, and transglutaminase having reactivity on the substrate improved by the method. In the present invention, the binding site of MTG for the substrate is extrapolated based on the three-dimensional structure obtained by X-ray crystal structure analysis of MTG crystals, and the mutant transglutaminases are designed and produced by replacing, inserting or deleting amino acid residues positioned at the substrate-binding site of the transglutaminase.

---------- KWIC ---------

Detail Description Paragraph - DETX (65):

[0141] When the subsequent amino acid of N-terminal Met is Ser, since N-terminal Met will be removed by methionine aminopeptidase of Escherichia coli, the codon corresponding to Ser may be positioned after the initiation

codon to prepare the Ser-type mutant having Ser at the N-terminal.

PGPUB-DOCUMENT-NUMBER: 20030224968

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030224968 A1

TITLE: Atlastin

PUBLICATION-DATE: December 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Fink, John K.	Ann Arbor	MI	US	
Zhao, Xinping	Houston	TX	US	

APPL-NO: 10/ 364748

DATE FILED: February 11, 2003

RELATED-US-APPL-DATA:

child 10364748 A1 20030211

parent continuation-in-part-of 10242008 20020912 US PENDING

non-provisional-of-provisional 60323997 20010921 US

US-CL-CURRENT: 514/1, 435/320.1 , 435/325 , 435/6 , 435/69.1 , 530/350 , 536/23.5 , 702/20

ABSTRACT:

The present invention relates to methods and compositions of a novel gene and the peptide encoded by the gene. Mutations in the gene, named atlastin, are factors in the disease Hereditary Spastic Paraplegia and related disorders. The present invention will be used for the in the research, diagnosis and treatment of these disabling diseases.

---------- KWIC ---------

Detail Description Paragraph - DETX (172):

[0210] In addition, the present invention provides fragments of atlastin (i.e., truncation mutants, e.g., portions of SEQ ID NOS:1, 3, 4 and 5). In other embodiments, the present invention provides domains of atlastin (e.g., the GTPase domain). In some embodiments of the present invention, when expression of a portion of the atlastin protein is desired, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol., 169:751) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1990) Proc. Natl. Acad. Sci. USA 84:2718). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing such recombinant polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP.

PGPUB-DOCUMENT-NUMBER: 20030220244

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030220244 A1

TITLE: Hedgehog signaling promotes the formation of three dimensional cartilage matrices, methods and compositions related thereto

PUBLICATION-DATE: November 27, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Warzecha, Joerg	Frankfurt		DE	

APPL-NO: 10/ 294036

DATE FILED: November 13, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60350594 20011113 US

US-CL-CURRENT: 514/12, 424/93.7 , 435/366

ABSTRACT:

The present invention provides methods and compositions for promoting the formation of three dimensional cartilage matrices. The present invention further provides methods of treating diseases and injuries involving cartilage and bone using the three dimensional cartilage matrices provided herein.

RELATED APPLICATIONS

[0001] This application claims priority to U.S. provisional application No. 60/350,594 filed Nov. 13, 2001, the disclosure of which is hereby incorporated by reference in its entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (60):

[0188] When it is desirable to express only a portion of an hedgehog protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing hedgehog-derived polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

PGPUB-DOCUMENT-NUMBER: 20030219740

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030219740 A1

TITLE: DNA sequences isolated from human colonic epithelial cells

PUBLICATION-DATE: November 27, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Boman, Bruce M.	Gladwyne	PA	US	
Wang, Laingjun	Plano	TX	US	

APPL-NO: 10/ 089887

DATE FILED: March 29, 2002

RELATED-US-APPL-DATA:

child 10089887 A1 20020329

parent continuation-of PCT/US00/21606 20000808 US PENDING

non-provisional-of-provisional 60147933 19990809 US

US-CL-CURRENT: 435/6, 435/320.1 , 435/325 , 435/69.1 , 435/7.1 , 530/350 , 536/23.5 , 800/14

ABSTRACT:

The present invention discloses novel nucleic acid sequences which are implicated in the growth regulation of the epithelial cells of the colon, and which sequences are differentially expressed in cancerous colon tissues compared to normal colon tissues. These sequences are useful in diagnosing abnormal cell growth, treatment of abnormal cell growth and screening assays for treatments of abnormal cell growth.

RELATED APPLICATIONS

[0001] This application is a continuation of International Application No. PCT/US00/21606, which designated the United States and was filed on Aug. 8, 2000, published in English, which claims the benefit of U.S. Provisional Application No. 60/147,933. The entire teachings of the above applications are incorporated herein by reference.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (164):

[0161] When it is desirable to express only a portion of a gene, e.g., a truncation mutant, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al., (1987) J. Bacteriol.

169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

PGPUB-DOCUMENT-NUMBER: 20030204070

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030204070 A1

TITLE: Polynucleotide encoding a novel methionine aminopeptidase, protease-39

PUBLICATION-DATE: October 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Chen, Jian	Princeton	NJ	US	
Feder, John N.	Belle Mead	NJ	US	
Nelson, Thomas C.	Lawrenceville	NJ	US	
Bassolino, Donna A.	Hamilton	NJ	US	
Krystek, Stanley R.	Ringoes	NJ	US	
Naglich, Joseph	Yardley	PA	US	

APPL-NO: 10/ 350516

DATE FILED: January 23, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60351251 20020123 US

non-provisional-of-provisional 60362872 20020308 US

US-CL-CURRENT: 536/23.2, 435/226 , 435/320.1 , 435/325 , 435/69.1

ABSTRACT:

The present invention provides novel polynucleotides encoding Protease-39 polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these novel Protease-39 polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

[0001] This application claims benefit to provisional application U.S. Serial No. 60/351,251 filed Jan. 23, 2002; and to provisional application U.S. Serial No. 60/362,872, filed Mar. 8, 2002. The entire teachings of the referenced applications are incorporated herein by reference.

---------- KWIC ---------

Detail Description Paragraph - DETX (118):

[0203] Also more preferred are polypeptides comprising all or any part of the Protease-39 methionine aminopeptidase domain, or a mutant or homologue of said polypeptide or molecular complex. By mutant or homologue of the molecule

is meant a molecule that has a root mean square deviation from the backbone atoms of said Protease-39 amino acids of not more than about 4.5 Angstroms, and preferably not more than about 3.5 Angstroms.

Detail Description Paragraph - DETX (127):

[0211] For purposes of the present invention, by "at least a portion of" is meant all or any part of the Protease-39 methionine aminopeptidase domain defined by the structure coordinates according to Table IV (e.g., fragments thereof). More preferred are molecules comprising all or any parts of the Protease-39 methionine aminopeptidase domain, according to Table IV, or a mutant or homologue of said molecule or molecular complex. By mutant or homologue of the molecule it is meant a molecule that has a root mean square deviation from the backbone atoms of said Protease-39 amino acids of not more than 4.5 Angstroms, and preferably not more than 3.5 Angstroms.

Detail Description Paragraph - DETX (161):

[0245] Genes encoding the members of the methionine aminopeptidase class are conserved between human and yeast. In yeast, deletion of a single methionine aminopeptidase gene (e.g. methionine aminopeptidase-1) affects cellular growth but is not lethal. This phenotype is observed because this mutant strain retains methionine aminopeptidase-2 activity. The reciprocal is also true, deletion of the methionine aminopeptidase-2 gene results in a slow growth phenotype but the cells do not die because they retain methionine aminopeptidase-1 activity. Consequently, a yeast-based screen can be developed and utilized to identify molecules that promote or inhibit methionine aminopeptidase activities. For example, if mutant yeast strains are treated with fumagillin, an inhibitor of methionine aminopeptidase-2 activities, the treatment is lethal to yeast lacking the methionine aminopeptidase-1 gene and is not lethal to isogenic wild type yeast. Thus, one emodiment of the invention encompasses a specific class of compounds that kill yeast lacking the methionine aminopeptidase-1 gene but do not kill isogenic wildtype yeast.

PGPUB-DOCUMENT-NUMBER: 20030203406

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030203406 A1

TITLE: Human methionine aminopeptidase type 3

PUBLICATION-DATE: October 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Sympson, Carolyn J.	Ballwin	MO	US	
Aurora, Rajeev	Glencoe	MO	US	
Dotson, Stanton B.	Chesterfield	MO	US	
Frazier, Ronald B.	Lake St. Louis	MO	US	
Woods, Cynthia L.	St. Peters	MO	US	
Zakeri, Hamideh	Chesterfield	MO	US	
Zhou, Xianzhi	Chesterfield	MO	US	

APPL-NO: 10/ 299867

DATE FILED: November 19, 2002

RELATED-US-APPL-DATA:

child 10299867 A1 20021119

parent continuation-in-part-of 09523263 20000310 US PENDING

non-provisional-of-provisional 60125139 19990311 US

US-CL-CURRENT: 435/7.1, 435/226 , 435/320.1 , 435/325 , 435/69.1 , 530/388.26 , 536/23.2

ABSTRACT:

Methionine aminopeptidases catalyse the co-translational removal of amino terminal methionine residues from nascent polypeptide chains. A newly-discovered enzyme, designated methionine aminopeptidase type-3 (MetAP-3), has a substrate specificity which is similar to MetAP-1 and MetAP-2, although it is not inhibited by fumagillin, an irreversible inhibitor of MetAP-2. MetAP-3 also preferentially localizes to mitochondria, unlike MetAP-1 and MetAP-2, which accumulate in the cytoplasm. One embodiment of the present invention relates to human cDNAs encoding polypeptides comprising MetAP-3. Other embodiments of the invention relate to nucleic acid molecules derived from these cDNAs, including complements, homologues, and fragments thereof, and methods of using these nucleic acid molecules, to generate polypeptides and fragments thereof. Other embodiments of the invention relate to antibodies directed against polypeptides comprising MetAP-3, and methods to screen for compounds or compositions that preferentially or specifically effect the activity of polypeptides comprising MetAP-3.

PRIORITY

[0001] The present application is a continuation-in-part of U.S. application Ser. No. 09/523,263, filed Mar. 10, 2000, pending, which claims priority under Title 35, United States Code .sctn.119, to U.S. Provisional Application

Serial No. 60/125,139, filed Mar. 11, 1999.

---------- KWIC ---------

Detail Description Paragraph - DETX (41):

[0129] Additionally, variant MetAP-3 proteins or fragments can be generated by known mutagenesis techniques so that one or more amino acids can be substituted, deleted, or added and the methionine aminopeptidase activity retained. Mutations that avoid or employ conservative substitutions within the known functional region, the C-terminal aminopeptidase domain, the residues that coordinate the cobalt ions, or domains possessing the same position in the amino acid chain as the aminopeptidase domain are preferred. Mutations that avoid changing amino acids at the known methionine aminopeptidase enzymatic active sites are also preferred. Methods to generate banks of mutant proteins, such as molecular evolution or DNA shuffling or the like, can be used. Assays for the methionine aminopeptidase activity that can identify these variant MetAP-3 molecules are also known. Such assays may involve an in vitro peptide substrate analysis (Freitas et al., Int. J. Biochem. 17:1285-1291 (1985), Xuo et al., Mol. Gen. Genet. 246:247-253 (1995), and Kendall and Bradshaw, J. Biol. Chem. 267:20667-10673 (1992)).

PGPUB-DOCUMENT-NUMBER: 20030199036

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030199036 A1

TITLE: Ubiquitin ligases, and uses related thereto

PUBLICATION-DATE: October 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
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Caligiuri, Maureen G.	Huntington	NY	US	
Nefsky, Bradley	Highland Park	NJ	US	

APPL-NO: 10/ 313955

DATE FILED: December 5, 2002

RELATED-US-APPL-DATA:

child 10313955 A1 20021205

parent continuation-of 09392163 19990908 US GRANTED

parent-patent 6503742 US

child 09392163 19990908 US

parent continuation-of 08539205 19951004 US GRANTED

parent-patent 6001619 US

US-CL-CURRENT: 435/69.1, 435/226 , 435/23 , 435/254.2 , 435/320.1 , 435/325 , 435/6 , 536/23.2 , 800/8

ABSTRACT:

The present invention relates to the discovery in eukaryotic cells of a ubiquitin ligases. These proteins are referred to herein collectively as "pub" proteins for Protein UBiquitin ligase, and individually as h-pub1, h-pub2 and s-pub1 for the human pub1 and pub2 and Schizosaccharomyces pombe pub1 clones, respectively. Pub1 proteins apparently play a role in the ubiquitination of the mitotic activating tyrosine phosphatase cdc25, and thus they may regulate the progression of proliferation in eukaryotic cells by activating the cyclin dependent kinase complexes. In S. pombe, disruption of s-pub1 elevates the level of cdc25 protein in vivo increasing the activity of the tyrosine kinases, wee1 and mik1, required to arrest the cell-cycle. Loss of weel function in an S. pombe cell carrying a disruption in the s-pub1 gene results in a lethal premature entry into mitosis; such lethal phenotype can be rescued by the loss of cdc25 function. An ubiquitin thioester adduct of s-pub1 can be isolated from S. pombe and disruption of s-pub1 dramatically reduces ubiquitination of cdc25.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (103):

[0100] When expression of a carboxy terminal fragment of the full-length pub proteins is desired, i.e. a truncation mutant, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al., (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al., (1987) Proc. Natl. Acad. Sci. USA 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing such recombinant polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al.).

PGPUB-DOCUMENT-NUMBER: 20030194783

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030194783 A1

TITLE: Co-administration of interleukin-3 mutant polypeptides with CSF's for multi-lineage hematopoietic cell production

PUBLICATION-DATE: October 16, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
McKearn, John P.	Glencoe	MO	US	
Olins, Peter	San Diego	CA	US	
Thomas, John	Potomac	MD	US	
Caparon, Maire	Chesterfield	MO	US	
Easton, Alan	Maryland Heights	MO	US	
Klein, Barbara	St. Louis	MO	US	
Bauer, S. Christopher	New Haven	MO	US	
Abrams, Mark	St. Louis	MO	US	
Paik, Kumnan	Chesterfield	MO	US	
Braford-Goldberg, Sarah			US	

APPL-NO: 10/ 072571

DATE FILED: February 8, 2002

RELATED-US-APPL-DATA:

child 10072571 A1 20020208

parent continuation-of 08446871 19950606 US GRANTED

parent-patent 6361976 US

child 08446871 19950606 US

parent continuation-in-part-of 08193373 19940204 US GRANTED

parent-patent 6153183 US

child 08193373 19940204 US

parent continuation-in-part-of PCT/US93/11197 19931122 US UNKNOWN

child PCT/US93/11197 19931122 US

parent continuation-in-part-of 07981044 19921124 US ABANDONED

US-CL-CURRENT: 435/69.52, 435/320.1 , 435/325 , 530/351 , 536/23.5

ABSTRACT:

The present invention relates to human interleukin-3 (hIL-3) variant or mutant proteins (muteins) functionally co-administered with a other colony stimulating factors (CSF), cytokines, lymphokines, interleukins, hematopoietic growth

factors or IL-3 variants.

---------- KWIC ---------

Detail Description Paragraph - DETX (30):

[0059] Suitable cells or cell lines for the production of the proteins claimed in the present invention may be bacterial cells. For example, the various strains of E. coli are well-known as host cells in the field of biotechnology. Examples of such strains include E. coli strains JM101 [Yanish-Perron, et al. (1985)] and MON105 [Obukowicz, et al. (1992)]. Also included in the present invention is the expression of the IL-3 variant protein utilizing a chromosomal expression vector for E. coli based on the bacteriophage Mu (Weinberg et al., 1993). Various strains of B. subtilis may also be employed as host cells for expression of the polypeptides of the present invention. Many strains of yeast cells known to those skilled in the art are also available as host cells for expression of the polypeptides of the present invention. When expressed in the E. coli cytoplasm, the above-mentioned mutant hIL-3 variants of the present invention may also be constructed with Met-Ala- at the N-terminus so that upon expression the Met is cleaved off leaving Ala at the N-terminus. The IL-3 variant proteins of the present invention may include polypeptides having Met-, Ala- or Met-Ala- attached to the N-terminus. When the IL-3 variant polypeptides are expressed in the cytoplasm of E. coli, polypeptides with and without Met attached to the N-terminus are obtained. The N-termini of proteins made in the cytoplasm of E. coli are affected by posttranslational processing by methionine aminopeptidase (Ben-Bassat et al., 1987) and possibly by other peptidases. These IL-3 variant proteins may also be expressed in E. coli by fusing a signal peptide to the N-terminus. This signal peptide is cleaved from the polypeptide as part of the secretion process. Secretion in E. coli can be used to obtain the correct amino acid at the N-terminus (e.g., Asn.sup.15 in the (15-125) hIL-3 polypeptide) due to the precise nature of the signal peptidase. This is in contrast to the heterogeneity which may be observed at the N-terminus of proteins expressed in the cytoplasm in E. coli.

PGPUB-DOCUMENT-NUMBER: 20030190696

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030190696 A1

TITLE: Vertebrate tissue pattern-inducing proteins, and uses related thereto

PUBLICATION-DATE: October 9, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ingham, Philip W.	Summertown		GB	
McMahon, Andrew P.	Lexington	MA	US	
Tabin, Clifford J.	Cambridge	MA	US	
Bumcrot, David A.	Belmont	MA	US	
Marti-Gorostiza, Elisa	Brookline		US	

APPL-NO: 09/ 736476

DATE FILED: December 13, 2000

RELATED-US-APPL-DATA:

child 09736476 A1 20001213

parent continuation-of 08460900 19950605 US GRANTED

parent-patent 6165747 US

child 08460900 19950605 US

parent continuation-in-part-of 08435093 19950504 US ABANDONED

child 08435093 19950504 US

parent continuation-in-part-of 08356060 19941214 US GRANTED

parent-patent 5844079 US

child 08356060 19941214 US

parent continuation-in-part-of 08176427 19931230 US GRANTED

parent-patent 5789543 US

US-CL-CURRENT: 435/69.1, 435/320.1 , 435/325 , 530/350 , 536/23.5

ABSTRACT:

The present invention concerns the discovery that proteins encoded by a family of vertebrate genes, termed here hedgehog-related genes, comprise morphogenic signals produced by tissue patterning centers, and are involved in the formation of ordered spatial arrangements of differentiated tissues in vertebrates. The present invention makes available compositions and methods that can be utilized, for example to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

RELATED APPLICATIONS

[0001] This application is a continuation-in-part of U.S. Ser. No. 08/435,093, filed May 4, 1995, which is a continuation-in-part of U.S. Ser. No. 08/356,060, filed Dec. 14, 1994, which is a continuation-in-part of U.S. Ser. No. 08/227,371 filed Dec. 30, 1993, the teachings of each of which are incorporated herein by reference.

---------- KWIC ---------

Detail Description Paragraph - DETX (79):

[0136] When it is desirable to express only a portion of a hedgehog protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing hedgehog-derived polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

PGPUB-DOCUMENT-NUMBER: 20030186357

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030186357 A1

TITLE: VERTEBRATE EMBRYONIC PATTERN-INDUCING PROTEINS, AND USES RELATED THERETO

PUBLICATION-DATE: October 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
INGHAM, PHILIP W.	SUMMERTOWN	MA	GB	
MCMAHON, ANDREW P.	LEXINGTON	MA	US	
TABIN, CLIFFORD J.	CAMBRIDGE		US	

APPL-NO: 08/ 462386

DATE FILED: June 5, 1995

CONTINUED PROSECUTION APPLICATION: This is a publication of a continued prosecution application (CPA) filed under 37 CFR 1.53(d).

RELATED-US-APPL-DATA:

child 08462386 A1 19950605

parent continuation-in-part-of 08435093 19950504 US ABANDONED

child 08435093 19950504 US

parent continuation-in-part-of 08356060 19941214 US GRANTED

parent-patent 5844079 US

child 08356060 19941214 US

parent continuation-in-part-of 08176427 19931230 US GRANTED

parent-patent 5789543 US

US-CL-CURRENT: 435/69.1, 435/320.1 , 435/325

ABSTRACT:

The present invention concerns the discovery that proteins encoded by a family of vertebrate genes, termed here hedgehog-related genes, comprise morphogenic signals produced by embryonic patterning centers, and are involved in the formation of ordered spatial arrangements of differentiated tissues in vertebrates. The present invention makes available compositions and methods that can be utilized, for example to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

RELATED APPLICATIONS

[0001] This application is a continuation-in-part of U.S. Ser. No. 08/435,093, filed May 4, 1995, which is a continuation-in-part of U.S. Ser.

No. Ser. No. 08/356,060, filed Dec. 14, 1994, which is a continuation-in-part of U.S. Ser. No. Ser. No. 08/227,371 filed Dec. 30, 1993 and entitled "Vertebrate Embryonic Pattern-Inducing Proteins and Uses Related Thereto", the teachings of which are incorporated herein by reference.

---------- KWIC ---------

Detail Description Paragraph - DETX (84):

[0144] When it is desirable to express only a portion of an hh protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing hedgehog-derived polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

PGPUB-DOCUMENT-NUMBER: 20030180737

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030180737 A1

TITLE: Method of reverse transcription

PUBLICATION-DATE: September 25, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Gu, Trent	Madison	WI	US	
Huang, Fen	Madison	WI	US	
Hartnett, James Robert	Madison	WI	US	

APPL-NO: 10/ 178673

DATE FILED: June 24, 2002

RELATED-US-APPL-DATA:

child 10178673 A1 20020624

parent continuation-of 09517871 20000302 US GRANTED

parent-patent 6436677 US

US-CL-CURRENT: 435/6, 435/91.2

ABSTRACT:

The present invention relates to reverse transcription of RNA, and in particular to reverse transcription by thermostable DNA polymerases. Thermoactinoinyces vulgaris and Bacillus stearothermophilus possess reverse transcriptase activity in the presence of magnesium or manganese ions. Methods, compositions, and kits for reverse transcription and RT-PCR are also provided.

---------- KWIC ---------

Detail Description Paragraph - DETX (113):

[0136] The present invention further provides fragments of Tvu DNA polymerase (i.e., deletion mutants; e.g., SEQ ID NOs 4 and 6). In some embodiments of the present invention, when expression of a portion of Tvu DNA polymerase is desired, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al., J. Bacteriol., 169:751-757, 1987) and S. typhimurium, and its in vitro activity has been demonstrated on recombinant proteins (Miller et al., Proc. Nat'l. Acad. Sci., 84:2718-1722, 1990). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing such recombinant polypeptides in a host producing MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP.

PGPUB-DOCUMENT-NUMBER: 20030175911

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030175911 A1

TITLE: Process for the preparation of L-amino acids with amplification of the zwf gene

PUBLICATION-DATE: September 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hans, Stephen	Osnabruek		DE	
Bathe, Brigitte	Salzkotten		DE	
Reth, Alexander	Bielefeld		DE	
Thierbach, Georg	Bielefeld		DE	
Kreutzer, Caroline	Melle		DE	
Mockel, Bettina	Dusseldorf		DE	

APPL-NO: 10/ 336049

DATE FILED: January 3, 2003

RELATED-US-APPL-DATA:

child 10336049 A1 20030103

parent continuation-in-part-of 10091342 20020306 US PENDING

child 10091342 20020306 US

parent continuation-in-part-of 09531269 20000320 US ABANDONED

US-CL-CURRENT: 435/115, 435/252.3

ABSTRACT:

The invention relates to a process for the preparation of L-amino acids by the fermentation of coryneform bacteria. The process involves: fermenting an L-amino acid-producing bacteria in which at least the zwf gene is amplified; concentrating the L-amino acid in the medium or in the cells of the bacteria; and isolating the L-amino acid produced.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] The present application is a continuation-in-part of U.S. Ser. No. 10/091,342, filed on Mar. 6, 2002, which is a continuation-in-part of U.S. Ser. No. 09/531,269, filed Mar. 20, 2000.

---------- KWIC ---------

Detail Description Paragraph - DETX (41):

[0053] In a further aspect of the invention, it has been found that amino acid exchanges in the section between position 369 and 373 and/or position 241 and 246 of the amino acid sequence of the zwf gene product, as shown in SEQ ID NO: 10, amplify its glucose 6-phosphate dehydrogenase activity. This appears

to be due to a decrease in the susceptibility of the enzyme to inhibition by NADPH (nicotinamide adenine dinucleotide phosphate, reduced form) resulting in an improvement in the production of amino acids, especially lysine, by coryneform bacteria. The methionine residue in the N-terminal position can be removed during post translational modification by a methionine aminopeptidase of the host. Accordingly, the invention provides Zwf proteins comprising the amino acid sequence of SEQ ID NO: 10, wherein at least one or more of the amino acids at positions 369 to 373 and/or one or more of the amino acids at positions 241 to 246 is (are) exchanged by another proteinogenic amino acid. In addition, the invention provides isolated polynucleotides encoding Zwf proteins containing these mutations.

PGPUB-DOCUMENT-NUMBER: 20030175762

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030175762 A1

TITLE: Modulators on Nod2 signaling

PUBLICATION-DATE: September 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Nunez, Gabriel	Ann Arbor	MI	US	
Inohara, Naohiro	Ann Arbor	MI	US	
Ogura, Yasunori	Ann Arbor	MI	US	

APPL-NO: 10/ 314506

DATE FILED: December 9, 2002

RELATED-US-APPL-DATA:

child 10314506 A1 20021209

parent continuation-in-part-of 10014269 20011026 US PENDING

non-provisional-of-provisional 60244289 20001030 US

US-CL-CURRENT: 435/6, 435/7.21 , 514/8

ABSTRACT:

The present invention relates to intracellular signaling molecules, in particular the Nod2 protein and nucleic acids encoding the Nod2 protein. The present invention provides methods of identifying modulators of Nod2 signaling. In particular, the present invention additionally provides methods of screening immune modulators such as adjuvants using Nod2. The present invention further provides methods of altering Nod2 signaling.

[0001] This application is a continuation in part of U.S. patent application Ser. No. 10/014,269, filed Oct. 26, 2001, which claims priority to U.S. provisional patent application serial No. 60/244,289, filed Oct. 30, 2000, each of which is herein incorporated by reference in its entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (140):

[0183] In addition, the present invention provides fragments of Nod2 (i.e., truncation mutants, e.g., SEQ ID NO:3). In some embodiments of the present invention, when expression of a portion of the Nod2 protein is desired, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al., J. Bacteriol., 169:751-757 [1987]) and

Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al., Proc. Natl. Acad. Sci. USA 84:2718-1722 [1990]). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing such recombinant polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP.

PGPUB-DOCUMENT-NUMBER: 20030165873

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030165873 A1

TITLE: Three hybrid assay system

PUBLICATION-DATE: September 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Come, Jon H.	Cambridge	MA	US	
Becker, Frank	Planegg	MA	DE	
Kley, Nikolai	Wellesley		US	

APPL-NO: 10/ 091177

DATE FILED: March 4, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60272932 20010302 US

non-provisional-of-provisional 60278233 20010323 US

non-provisional-of-provisional 60329437 20011015 US

US-CL-CURRENT: 435/6, 435/7.1 , 530/350 , 536/23.1 , 536/5 , 552/570

ABSTRACT:

The invention provides compositions and methods for isolating ligand binding polypeptides for a user-specified ligand, and for isolating small molecule ligands for a user-specified target polypeptide using an improved class of hybrid ligand compounds.

REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional application No. 60/272,932, filed on Mar. 2, 2001; U.S. Provisional application No. 60/278,233, filed on Mar. 23, 2001; and U.S. Provisional application No. 60/329,437, filed on Oct. 15, 2001, the specifications of which are hereby incorporated by reference in their entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (292):

[0379] When it is desirable to express only a portion of a protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its ire vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722).

Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing polypeptides in a host which produces MAP (e.g., E. coli ox CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

PGPUB-DOCUMENT-NUMBER: 20030162698

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030162698 A1

TITLE: METHODS AND COMPOSITIONS FOR TREATING DOPAMINERGIC AND GABA-NERGIC DISORDERS

PUBLICATION-DATE: August 28, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
GALDES, ALPHONSE	LEXINGTON	MA	US	
MAHANTHAPPA, NAGESH	CAMBRIDGE	MA	US	

APPL-NO: 09/ 238243

DATE FILED: January 27, 1999

CONTINUED PROSECUTION APPLICATION: This is a publication of a continued prosecution application (CPA) filed under 37 CFR 1.53(d).

US-CL-CURRENT: 514/12, 530/359

ABSTRACT:

It is shown here that hedgehog proteins possess novel activities beyond phenotype specification. Using cultures derived from the embryonic day 14.5 (E14.5) rat ventral mesencephalon, we show that hedgehog is also trophic for dopaminergic neurons. Interestingly, hedgehog not only promotes dopaminergic neuron survival, but also promotes the survival of midbrain GABA-immunoeractive (GABA-ir) neurons. In animal models, hedgehog polypeptides are potent protective and restorative agents for lesions involving substantia nigra structures.

---------- KWIC ---------

Detail Description Paragraph - DETX (107):

[0142] When it is desirable to express only a portion of a hedgehog protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing hedgehog-derived polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

PGPUB-DOCUMENT-NUMBER: 20030148420

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030148420 A1

TITLE: Aspergillus ochraceus 11 alpha hydroxylase and oxidoreductase

PUBLICATION-DATE: August 7, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Suzanne, Bolten L.	Kirkwood	MO	US	
Clayton, Robert A.	Foristell	MO	US	
Easton, Alan M.	Maryland Height	MO	US	
Engel, Leslie C.	Des Pere	MO	US	
Messing, Dean M.	St. Louis	MO	US	
Ng, John S.	Oak Park	CA	US	
Reitz, Beverly	Chesterfield	MO	US	
Walker, Mark C.	Chesterfield	MO	US	
Wang, Ping T.	Manchester	MO	US	

APPL-NO: 10/ 021425

DATE FILED: October 30, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60244300 20001030 US

US-CL-CURRENT: 435/69.1, 435/189 , 435/254.2 , 435/320.1 , 435/6 , 435/60 , 536/23.2

ABSTRACT:

The present invention relates to a novel cytochrome P450-like enzyme (Aspergillus ochraceus 11 alpha hydroxylase) and an oxidoreductase (Aspergillus ochraceus oxidoreductase) isolated from cDNA library generated from the mRNA of Aspergillus ochraceus spores. When the cDNA encoding the 11 alpha hydroxylase was co-expressed in Spodoptera frugiperda (Sf-9) insect cells with the cDNA encoding human oxidoreductase as an electron donor, it successfully catalyzed the conversion of the steroid substrate 4-androstene-3,17-dione (AD) to 11 alpha-hydroxy-AD as determined by HPLC analysis. The invention also relates to nucleic acid molecules associated with or derived from these cDNAs including complements, homologues and fragments thereof, and methods of using these nucleic acid molecules, to generate, for example, polypeptides and fragments thereof. The invention also relates to the generation of antibodies that recognizes the A. ochraceus 11 alpha hydroxylase and oxidoreductase and methods of using these antibodies to detect the presence of these native and recombinant polypeptides within unmodified and transformed host cells, respectively. The invention also provides methods of expressing the Aspergillus 11 alpha hydroxylase gene separately, or in combination with human or Aspergillus oxidoreductase, in heterologous host cells, to facilitate the bioconversion of steroid substrates to their 11 alpha hydroxy-counterparts.

PRIORITY

[0001] The present application claims priority under Title 35, United States Code, .sctn.119 of U.S. Provisional Application Serial No. 60/244,300, filed Oct. 30, 2000.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (183):

[0179] When expressed in the E. coli cytoplasm, the gene encoding the proteins of the present invention may also be constructed such that at the 5' end of the gene codons are added to encode Met.sup.-2--Ala.sup.-1, Met.sup.-2--Ser.sup.-1, Met.sup.-2--Cys.sup.-1, or Met.sup.-1 at the N-terminus of the protein. The N termini of proteins made in the cytoplasm of E. coli are affected by post-translational processing by **methionine aminopeptidase** (Ben Bassat et al., J. Bacteriol. 169:751-757, 1987), and possibly by other peptidases, so that upon expression the **methionine** is cleaved off the N-terminus. The proteins of the present invention may include polypeptides having Met.sup.-1, Ala.sup.-1, Ser.sup.-1, Cys.sup.-1, Met.sup.-2--Ala.sup.-1, Met.sup.-2--Ser.sup.-1, or Met.sup.-2--Cys.sup.-1 at the N-terminus. These **mutant** proteins may also be expressed in E. coli by fusing a secretion signal peptide to the N-terminus. This signal peptide is cleaved from the polypeptide as part of the secretion process.

US-PAT-NO: 6664075

DOCUMENT-IDENTIFIER: US 6664075 B2

TITLE: Nucleic acids encoding hedgehog proteins

DATE-ISSUED: December 16, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ingham; Philip W.	Summertown	N/A	N/A	GB
McMahon; Andrew P.	Lexington	MA	N/A	N/A
Tabin; Clifford J.	Cambridge	MA	N/A	N/A
Bumcrot; David A.	Belmont	MA	N/A	N/A
Marti-Gorostiza; Elisa	Brookline	MA	N/A	N/A

APPL-NO: 09/ 736476

DATE FILED: December 13, 2000

PARENT-CASE:

RELATED APPLICATIONS

This application is a continuation of U.S. Ser. No. 08/460,900, filed Jun. 5, 1995, now U.S. Pat. No. 6,165,747, which is a continuation-in-part of U.S. Ser. No. 08/435,093, filed May 4, 1995 now abandoned, which is a continuation-in-part of U.S. Ser. No. 08/356,060, filed Dec. 14, 1994 now U.S. Pat. No. 5,844,079, which is a continuation-in-part of U.S. Ser. No. 08/176,427 filed Dec. 30, 1993 now U.S. Pat. No. 5,789,543, the teachings of each of which are incorporated herein by reference.

US-CL-CURRENT: 435/69.1, 435/252.3 , 435/254.11 , 435/320.1 , 435/325 , 435/69.7 , 530/300 , 530/350 , 536/23.1 , 536/23.4 , 536/23.5

ABSTRACT:

The present invention concerns the discovery that proteins encoded by a family of vertebrate genes, termed here hedgehog-related genes, comprise morphogenic signals produced by tissue patterning centers, and are involved in the formation of ordered spatial arrangements of differentiated tissues in vertebrates. The present invention makes available compositions and methods that can be utilized, for example to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

35 Claims, 19 Drawing figures

Exemplary Claim Number: 20

Number of Drawing Sheets: 19

---------- KWIC ---------

Detailed Description Text - DETX (79):
When it is desirable to express only a portion of a hedgehog protein, such

as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing hedgehog-derived polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

US-PAT-NO: 6656709

DOCUMENT-IDENTIFIER: US 6656709 B1

TITLE: Methods of increasing the production of cobalamins using cob gene expression

DATE-ISSUED: December 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Blanche; Francis	Paris	N/A	N/A	FR
Cameron; Beatrice	Paris	N/A	N/A	FR
Crouzet; Joel	Paris	N/A	N/A	FR
Debussche; Laurent	Paris	N/A	N/A	FR
Levy Schil; Sophie	Paris	N/A	N/A	FR
Thibaut; Denis	Paris	N/A	N/A	FR

APPL-NO: 08/ 426630

DATE FILED: April 21, 1995

PARENT-CASE:

This is a continuation of application Ser. No. 07/916,151, filed on Sep. 14, 1992 now abandoned which is a 371 of PCT/FR91/00054 filed Jan. 30, 1991.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
FR	90 01137	January 31, 1990

US-CL-CURRENT: 435/86

ABSTRACT:

Novel polypeptides involved in the biosynthesis of cobalamines and/or cobamides, in particular coenzyme B.sub.12, genetic material responsible for expressing these polypeptides, and a method for preparing them, are described. A method for amplifying the production of cobalamines, and particularly coenzyme B.sub.12, using recombinant DNA techniques, are also described.

58 Claims, 191 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 189

---------- KWIC ---------

Detailed Description Text - DETX (153):

The NH.sub.2 -terminal sequence of the COBH protein (FIG. 16) corresponds exactly to this sequence except that, in the sequence presented in FIG. 16, a methionine precedes the peptide sequence determined by the sequencing described above. It follows from this that the amino-terminal methionine is definitely excised in vivo by methionine aminopeptidase (Ben Bassat and Bauer, 1987). Since the second residue is a proline, this excision is in keeping with the

rules already stated (Hirel et al., 1989). The molecular weight of the purified precorrin-8x mutase, estimated by 12.5% SDS-PAGE electrophoresis, is 22,000. The COBH protein has a molecular weight deduced from its sequence of 22,050 (FIG. 16). The correspondences between the NH.sub.2 -terminal sequences and the molecular weights of these proteins indicate clearly that the COBH protein corresponds to precorrin-8x mutase. cobH is the precorrin-8x mutase structural gene.

US-PAT-NO: 6653098

DOCUMENT-IDENTIFIER: US 6653098 B1

TITLE: Method of producing mouse and human endostatin

DATE-ISSUED: November 25, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Violand; Bernard N.	Glencoe	MO	N/A	N/A
Harding; Elizabeth I.	Kirkwood	MO	N/A	N/A

APPL-NO: 09/ 231077

DATE FILED: January 14, 1999

PARENT-CASE:

PRIORITY

The present application claims priority under Title 35, United States Code, .sctn.119 of U.S. Provisional Application Serial No. 60/075,587 filed Feb. 23, 1998.

US-CL-CURRENT: 435/69.1, 435/252.33 , 435/252.5 , 435/254.2 , 435/320.1 , 435/325 , 435/348 , 435/366 , 530/350 , 536/23.1

ABSTRACT:

Methods for producing mouse and human endostatin are disclosed. Methods for refolding and purifying endostatin from inclusion bodies expressed in bacteria and nucleic acids encoding full-length and truncated forms of endostatin are also disclosed.

26 Claims, 18 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 10

---------- KWIC ---------

Brief Summary Text - BSTX (50):

When expressed in the E. coli cytoplasm, the gene encoding the proteins of the present invention may also be constructed such that at the 5' end of the gene codons are added to encode Met.sup.-2 -Ala.sup.-1, Met.sup.-2 -Ser.sup.-1, Met.sup.-2 -Cys.sup.-1, or Met.sup.-1 at the N-terminus of the protein. The N termini of proteins made in the cytoplasm of E. coli are affected by post-translational processing by methionine aminopeptidase (Ben Bassat et al., J. Bacteriol. 169:751-757, 1987) and possibly by other peptidases so that upon expression the methionine is cleaved off the N-terminus. The proteins of the present invention may include polypeptides having Met.sup.-1, Ala.sup.-1, Ser.sup.-1, Cys.sup.-1, Met.sup.-2 -Ala.sup.-1, Met.sup.-2 -Ser.sup.-1, or Met.sup.-2 -Cys.sup.-1 at the N-terminus. These mutant proteins may also be expressed in E. coli by fusing a secretion signal peptide to the N-terminus.

This signal peptide is cleaved from the polypeptide as part of the secretion process.

US-PAT-NO: 6639051

DOCUMENT-IDENTIFIER: US 6639051 B2

TITLE: Regulation of epithelial tissue by hedgehog-like polypeptides, and formulations and uses related thereto

DATE-ISSUED: October 28, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wang; Elizabeth A.	Carlisle	MA	N/A	N/A

APPL-NO: 09/ 151999

DATE FILED: September 11, 1998

PARENT-CASE:

REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. Ser. No. 08/955,552, filed Oct. 20, 1997, and now abandoned, the specification of which is incorporated by reference herein.

US-CL-CURRENT: 530/350, 424/198.1 , 530/300 , 530/324

ABSTRACT:

The invention provides methods and compositions for modulating hair growth.

28 Claims, 3 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 3

---------- KWIC ---------

Detailed Description Text - DETX (139):

When it is desirable to express only a portion of an hedgehog protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing hedgehog-derived polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

US-PAT-NO: 6638750

DOCUMENT-IDENTIFIER: US 6638750 B1

TITLE: Methionine aminopeptidase type 3

DATE-ISSUED: October 28, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Aurora; Rajeev	Chesterfield	MO	N/A	N/A
Dotson; Stanton B.	Fenton	MO	N/A	N/A

APPL-NO: 09/ 523263

DATE FILED: March 10, 2000

PARENT-CASE:

PRIORITY

The present application, claims priority under Title 35, United States Code, .sctn. 119 of U.S. Provisional Application Ser. No. 60/125,139, filed Mar. 11, 1999.

US-CL-CURRENT: 435/212, 435/252.3 , 435/320.1 , 530/300 , 530/350 , 536/23.2 , 536/23.6

ABSTRACT:

The present invention relates to a human cDNA encoding a methionine aminopeptidase type-3 (MetAP-3) protein. The invention also relates to nucleic acid molecules associated with or derived from this cDNA including complements, homologues and fragments thereof, and methods of using these nucleic acid molecules, to generate, for example, polypeptides and fragments thereof. The invention also provides methods of using the nucleic acids, for example, to produce a protein and fragments thereof and to screen for compounds or compositions that preferentially or specifically effect the activity of a MetAP-3 protein.

7 Claims, 26 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 26

---------- KWIC ---------

Detailed Description Text - DETX (67):

Additionally, variant MetAP-3 proteins or fragments can be generated by known mutagenesis techniques so that one or more amino acids can be substituted, deleted, or added and the methionine aminopeptidase activity retained. Mutations that avoid or employ conservative substitutions within the known functional region, the C-terminal aminopeptidase domain, the residues that coordinate the cobalt ions, or domains possessing the same position in the amino acid chain as the aminopeptidase domain are preferred. Mutations that

avoid changing amino acids at the known methionine aminopeptidase enzymatic active sites are also preferred. Methods to generate banks of mutant proteins, such as molecular evolution or DNA shuffling or the like, can be used. Assays for the methionine aminopeptidase activity that can identify these variant MetAP-3 molecules are also known. Such assays may involve an in vitro peptide substrate analysis (Freitas et al., Int. J. Biochem. 17:1285-1291 (1985), Xuo et al., Mol. Gen. Genet. 246:247-253 (1995), and Kendall and Bradshaw, J. Biol. Chem. 267:20667-10673 (1992)).

US-PAT-NO: 6632645

DOCUMENT-IDENTIFIER: US 6632645 B1

TITLE: Thermophilic DNA polymerases from Thermoactinomyces vulgaris

DATE-ISSUED: October 14, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gu; Trent	Madison	WI	N/A	N/A
Huang; Fen	Madison	WI	N/A	N/A
Hartnett; James Robert	Madison	WI	N/A	N/A

APPL-NO: 09/ 517439

DATE FILED: March 2, 2000

US-CL-CURRENT: 435/194, 435/320.1 , 435/6 , 536/23.2

ABSTRACT:

The present invention provides compositions comprising thermostable DNA polymerases derived from hyperthermophilic eubacteria. In particular, the present invention comprises thermostable DNA polymerases from the hyperthermophilic eubacterial species Thermoactinomyces vulgaris. The present invention also provides methods for utilizing naturally-occurring and non-naturally-occurring forms of T. vulgaris DNA polymerase in sequencing, reverse transcription, and amplification reactions.

13 Claims, 8 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 8

---------- KWIC ---------

Detailed Description Text - DETX (105):

The present invention further provides fragments of Tvu DNA polymerase (i.e., deletion mutants; e.g., SEQ ID NOs 4 and 6). In some embodiments of the present invention, when expression of a portion of Tvu DNA polymerase is desired, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al., J. Bacteriol. 169:751-757, 1987) and S. typhimurium, and its in vitro activity has been demonstrated on recombinant proteins (Miller et al., PNAS 84:2718-1722, 1990). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing such recombinant polypeptides in a host producing MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP.

US-PAT-NO: 6630148

DOCUMENT-IDENTIFIER: US 6630148 B1
See image for Certificate of Correction

TITLE: Compositions comprising hedgehog proteins

DATE-ISSUED: October 7, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ingham; Philip W.	Summertown	N/A	N/A	GB
McMahon; Andrew P.	Lexington	MA	N/A	N/A
Tabin; Clifford J.	Cambridge	MA	N/A	N/A

APPL-NO: 08/ 954740

DATE FILED: October 20, 1997

PARENT-CASE:

RELATED APPLICATIONS

This application is a continuation of application Ser. No. 08/462,386, filed Jun. 5, 1995, which is a continuation-in-part of application Ser. No. 08/435,093, filed May 4, 1995, now abandoned, which is a continuation-in-part of application Ser. No. 08/356,060, filed Dec. 14, 1994, now U.S. Pat. No. 5,844,079, which is a continuation-in-part of application Ser. No. 08/176,427 filed Dec. 30, 1993, now U.S. Pat. No. 5,789,543, the teachings of each of which are incorporated herein by reference.

US-CL-CURRENT: 424/185.1, 424/422 , 435/69.1 , 514/12 , 514/7 , 514/8 , 530/350 , 530/402 , 536/23.5

ABSTRACT:

The present invention concerns the discovery that proteins encoded by a family of vertebrate genes, termed here hedgehog-related genes, comprise morphogenic signals produced by embryonic patterning centers, and are involved in the formation of ordered spatial arrangements of differentiated tissues in vertebrates. The present invention makes available compositions and methods that can be utilized, for example to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

52 Claims, 20 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 19

---------- KWIC ---------

Detailed Description Text - DETX (84):
When it is desirable to express only a portion of an hh protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks the signal peptide, it may be necessary to add a start codon (ATG) to the

oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing hedgehog-derived polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

US-PAT-NO: 6610656

DOCUMENT-IDENTIFIER: US 6610656 B1
See image for Certificate of Correction

TITLE: Method of promoting chondrocyte differentiation with hedgehog related polypeptides

DATE-ISSUED: August 26, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ingham; Philip W.	Summertown	N/A	N/A	GB
McMahon; Andrew P.	Lexington	MA	N/A	N/A
Tabin; Clifford J.	Cambridge	MA	N/A	N/A

APPL-NO: 08/ 954128

DATE FILED: October 20, 1997

PARENT-CASE:

RELATED APPLICATIONS

This application is a continuation-in-part of U.S. Ser. No. 08/435,093 filed May 4, 1995, abandoned which is a continuation-in-part of U.S. Ser. No. 08/356,060, filed Dec. 14, 1994, now U.S. Pat. No. 5,844,079 which is continuation-in-part of U.S. Ser. No. 08/176,427 filed Dec. 30, 1993 now U.S. Pat. No. 5,789,543 and entitled "Vertebrate Embryonic Pattern-Inducing Proteins and Uses Related Thereto", the teachings of which are incorporated herein by reference.

US-CL-CURRENT: 514/12, 435/69.1 , 514/2 , 530/300 , 530/350 , 536/23.1 , 536/23.5

ABSTRACT:

The present invention concerns the discovery that proteins encoded by a family of vertebrate genes, termed here hedgehog-related genes, comprise morphogenic signals produced by embryonic patterning centers, and are involved in the formation of ordered spatial arrangements of differentiated tissues in vertebrates. The present invention makes available compositions and methods that can be utilized, for example to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

27 Claims, 19 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 19

---------- KWIC ---------

Detailed Description Text - DETX (84):
When it is desirable to express only a portion of an hh protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks

the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing hedgehog-derived polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

US-PAT-NO: 6610497

DOCUMENT-IDENTIFIER: US 6610497 B1

TITLE: Angiotensin converting enzyme homolog and therapeutic and diagnostic uses therefor

DATE-ISSUED: August 26, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Acton; Susan L.	Lexington	MA	N/A	N/A
Robison; Keith Earl	Wilmington	MA	N/A	N/A
Hsieh; Frank Y.	Lexington	MA	N/A	N/A

APPL-NO: 09/ 407427

DATE FILED: September 29, 1999

PARENT-CASE:

This application is a continuation-in-part of application Ser. No. 09/163,648, filed Sep. 30, 1998, which is a continuation-in-part of applicatipon Ser. No. 08/989,299, filed Dec. 11, 1997.

US-CL-CURRENT: 435/7.1, 436/501 , 436/86 , 530/313

ABSTRACT:

The present invention relates to the discovery of novel genes encoding an angiotensin converting enzyme, Angiotensin Converting Enzyme-2 (ACE-2). The invention provides therapeutics, prognostic and diagnostics methods for treating blood pressure related disorders as well as various types of allergic conditions, among others. Also disclosed are screening assays for identifying compounds for treating and preventing these conditions.

25 Claims, 21 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 17

---------- KWIC ---------

Detailed Description Text - DETX (129):

When it is desirable to express only a portion of an ACE-2 protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing ACE-2 derived polypeptides in a host which

produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in, vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

US-PAT-NO: 6607913

DOCUMENT-IDENTIFIER: US 6607913 B1

TITLE: Vertebrate embryonic pattern-inducing proteins and uses related thereto

DATE-ISSUED: August 19, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ingham; Philip W.	Summertown, Oxford	OX27L	N/A	GB
McMahon; Andrew P.	Lexington	MA	02173	N/A
Tabin; Clifford J.	Cambridge	MA	02138	N/A

APPL-NO: 09/ 448188

DATE FILED: November 23, 1999

PARENT-CASE:

RELATED APPLICATIONS

This application is a continuation of application Ser. No. 08/954,128, filed on Oct. 20, 1997, which is a continuation of application Ser. No. 08/462,386, filed on Jun. 5, 1995, which is a continuation-in-part of application Ser. No. 08/435,093, filed on May 4, 1995, continuation-in-part of application Ser. No. 08/356,060, filed Dec. 14, 1994 now U.S. Pat. No. 5,844,079, which is a continuation-in-part of application Ser. No. 08/176,427, filed Dec. 30, 1993 now U.S. Pat. No: 5,789,543.

US-CL-CURRENT: 435/325, 435/252.3 , 435/254.11 , 435/320.1 , 435/69.1 , 435/69.4 , 514/12 , 514/2 , 530/300 , 530/350 , 536/23.1 , 536/23.4 , 536/23.5

ABSTRACT:

The present invention concerns the discovery that proteins encoded by a family of vertebrate genes, termed here hedgehog-related genes, comprise morphogenic signals produced by embryonic patterning centers, and are involved in the formation of ordered spatial arrangements of differentiated tissues in vertebrates. The present invention makes available compositions and methods that can be utilized, for example to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

36 Claims, 20 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 19

---------- KWIC ---------

Detailed Description Text - DETX (84):

When it is desirable to express only a portion of an hh protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks

the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing hedgehog-derived polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of purified MAP (e.g., procedure of Miller et al., supra).

US-PAT-NO: 6605700

DOCUMENT-IDENTIFIER: US 6605700 B2

TITLE: Human patched genes and proteins, and uses related thereto

DATE-ISSUED: August 12, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bumcrot; David A.	Belmont	MA	N/A	N/A

APPL-NO: 09/ 909280

DATE FILED: July 19, 2001

PARENT-CASE:

This application is a Divisional of U.S. application Ser. No. 09/207,857, now U.S. Pat. No. 6,309,879, filed on Dec. 8, 1998, and claims benefit to U.S. Application 60/067,940, filed on Dec. 8, 1997, the specifications of which are hereby incorporated by reference in their entirety.

US-CL-CURRENT: 530/350, 536/23.5

ABSTRACT:

The present invention relates to the discovery of a new member of the hedgehog receptor family, referred to herein as human ptc-2 (for patched-2 protein). The human ptc-2 polypeptides of the present invention include polypeptides which bind the products of the hedgehog gene family. Hedgehog family members are known for their broad involvement in the formation and maintenance of ordered spatial arrangements of differentiated tissues in vertebrates, both adult and embryonic, and can be used to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

4 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Brief Summary Text - BSTX (99):

When it is desirable to express only a portion of a ptc-2 protein, such as a form lacking a portion of the N-terminus, i.e. a truncation mutant which lacks the signal peptide, it may be necessary to add a start codon (ATG) to the oligonucleotide fragment containing the desired sequence to be expressed. It is well known in the art that a methionine at the N-terminal position can be enzymatically cleaved by the use of the enzyme methionine aminopeptidase (MAP). MAP has been cloned from E. coli (Ben-Bassat et al. (1987) J. Bacteriol. 169:751-757) and Salmonella typhimurium and its in vitro activity has been demonstrated on recombinant proteins (Miller et al. (1987) PNAS 84:2718-1722). Therefore, removal of an N-terminal methionine, if desired, can be achieved either in vivo by expressing ptc-2-derived polypeptides in a host which produces MAP (e.g., E. coli or CM89 or S. cerevisiae), or in vitro by use of

purified MAP (e.g., procedure of Miller et al., supra).

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	441	methionine adj aminopeptidase$	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:38
L2	7079	(methionine or met) same muta$10	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:38
L3	185	1 same 2	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:39
L4	1908	methionine same cysteine same muta$10	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:17
L5	102	4 same stab$8	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:18

PGPUB-DOCUMENT-NUMBER: 20040033487

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040033487 A1

TITLE: Modifications of HIV Env, Gag, and Pol enhance immunogenicity for genetic immunization

PUBLICATION-DATE: February 19, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Nabel, Gary J.	Washington	DC	US	
Chakrabarti, Bimal K.	Gaithersburg	MD	US	
Huang, Yue	Gaithersburg	MD	US	

APPL-NO: 10/ 359120

DATE FILED: February 4, 2003

RELATED-US-APPL-DATA:

child 10359120 A1 20030204

parent continuation-of PCT/US01/25721 20010814 US PENDING

non-provisional-of-provisional 60279257 20010328 US

non-provisional-of-provisional 60252115 20001114 US

non-provisional-of-provisional 60225097 20000814 US

US-CL-CURRENT: 435/5, 435/235.1 , 435/320.1 , 435/325 , 435/69.3 , 530/395 , 536/23.72

ABSTRACT:

Modified HIV Env, Gag, Pol, or Nef DNA with improved ability to elicit antibody and CTL responses to HIV antigens have been identified as prototype immunogens for the treatment and prevention of HIV infections.

I. CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation of international application number PCT/US01/25721, and claims the benefit of priority of international application number PCT/US01/25721 having international filing date of Aug. 14, 2001, designating the United States of America and published in English, which claims the benefit of priority of U.S. provisional patent application No. 60/279,257, filed Mar. 28, 2001, U.S. provisional patent application No. 60/252,115, filed Nov. 14, 2000, and U.S. provisional patent application No. 60/225,097, filed Aug. 14, 2000; all of which are hereby expressly incorporated by reference in their entireties.

---------- KWIC ---------

Detail Description Paragraph - DETX (96):

[0137] Amino acid substitutions may encompass those of a conserved or non-conserved nature. Presumably, a non-conserved substitution of a domain would act like a deletion of the domain. Conserved amino acid substitutions constitute switching one or more amino acids with amino acids of similar charge, size, and/or hydrophobicity characteristics. Non-conserved amino acid substitutions constitute switching one or more amino acids with amino acids of dissimilar charge, size, and/or hydrophobicity characteristics. The families of amino acids include the basic amino acids (lysine, arginine, histidine); the acidic amino acids (aspartic acid, glutamic acid); the non-polar amino acids (alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan); the uncharged polar amino acids (glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine); and the aromatic amino acids (phenylalanine, tryptophan, and tyrosine). One or more substitutions may be introduced to achieve the .DELTA.C mutation intended to eliminate proteolysis by acting like a deletion of the gp120/gp41 cleavage site to link the envelope covalently to the ectodomain, the .DELTA.F mutation intended to solubilize the molecule by acting like a deletion of the fusion domain, the .DELTA.I mutation intended to stabilize oligomer formation by acting like a deletion of the interspace between the two heptad repeats, the COOH-terminal truncation intended to reduce toxicity by acting like a deletion of the cytoplasmic domain, and, optionally, the COOH-terminal truncation extended so as to solubilize the molecule by acting like a deletion of the transmembrane domain.

PGPUB-DOCUMENT-NUMBER: 20030219385

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030219385 A1

TITLE: Contrast agents for magnetic resonance imaging and methods related thereto

PUBLICATION-DATE: November 27, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ahrens, Eric	Pittsburgh	PA	US	

APPL-NO: 10/ 384496

DATE FILED: March 7, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60363163 20020307 US

US-CL-CURRENT: 424/9.322, 435/235.1 , 435/456 , 435/6 , 435/7.2 , 800/288 , 800/8

ABSTRACT:

In certain aspects the present invention provides methods and compositions related to contrast agents for magnetic resonance imaging. In certain variations, contrast agents provided herein are generated in situ via genetic instructions and become potent upon sequestering available metal atoms. Exemplary contrast agents include metal-binding proteins.

RELATED APPLICATIONS

[0001] This application claims the benefit of priority to U.S. Provisional Patent Application No. 60/363,163, filed on Mar. 7, 2002, which application is hereby incorporated by reference in its entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (50):

[0093] In further embodiments, contrast proteins of the invention may be engineered, by for example, employing techniques of molecular biology. For example, it is possible to modify the structure of the subject contrast proteins for such purposes as enhancing contrast efficacy, stability (e.g., increased or decreased resistance to proteolytic degradation in vivo), antigenicity, or safety, among other characteristics. Such modified proteins can be produced, for instance, by amino acid substitution, deletion, or addition. In addition, simple variants of any of the proteins discussed herein may be obtained by conservative substitution. For instance, it is reasonable to expect that an isolated replacement of a leucine with an isoleucine or valine, an aspartate with a glutamate, a threonine with a serine, or a similar replacement of an amino acid with a structurally related amino acid (i.e. conservative mutations) will not have a major effect on the biological activity of the resulting molecule. Conservative replacements are those that take place

within a family of amino acids that are related in their side chains. Genetically encoded amino acids are can be divided into four families: (1) acidic=aspartate, glutamate; (2) basic=lysine, arginine, histidine; (3) nonpolar=alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan; and (4) uncharged polar=glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine. Phenylalanine, tryptophan, and tyrosine are sometimes classified jointly as aromatic amino acids. In similar fashion, the amino acid repertoire can be grouped as (1) acidic=aspartate, glutamate; (2) basic=lysine, arginine histidine, (3) aliphatic=glycine, alanine, valine, leucine, isoleucine, serine, threonine, with serine and threonine optionally be grouped separately as aliphatic-hydroxyl; (4) aromatic=phenylalanine, tyrosine, tryptophan; (5) amide=asparagine, glutamine; and (6) sulfur-containing=cysteine and methionine. (see, for example, Biochemistry, 2nd ed., Ed. by L. Stryer, W. H. Freeman and Co., 1981).

PGPUB-DOCUMENT-NUMBER: 20030194743

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030194743 A1

TITLE: Binding polypeptides for B lymphocyte stimulator protein (BLyS)

PUBLICATION-DATE: October 16, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Beltzer, James P.	Carlisle	MA	US	
Potter, M. Daniel	Acton	MA	US	
Potter, Marilou	Acton	MA	US	
Fleming, Tony J.	Waltham	MA	US	
Ladner, Robert Charles	Ijamsville	MD	US	

APPL-NO: 09/ 932322

DATE FILED: August 17, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60226489 20000818 US

US-CL-CURRENT: 435/7.1, 435/235.1 , 530/327 , 530/328 , 536/23.1

ABSTRACT:

Binding polypeptides comprising specific amino acid sequences are disclosed that bind B Lymphocyte Stimulator (BLyS) protein or BLyS-like polypeptides. The binding polypeptides can be used in methods of the invention for detecting or isolating BLyS protein or BLyS-like polypeptides in solutions or mixtures, such as blood, tissue samples, or conditioned media.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (213):

[0210] A "BLyS binding polypeptide" is a molecule of the invention that can bind BLyS target protein. Non-limiting examples of BLyS binding polypeptides of the invention are the polypeptide molecules having an amino acid sequence described herein (see SEQ ID NOs: 1-12, 20-172, and 186-444). The term BLyS binding polypeptide also encompasses BLyS binding fragments and variants (including derivatives) of polypeptides having the specific amino acid sequences described herein (SEQ ID NOs: 1-12, 20-172, and 186-444). By "variant" of an amino acid sequence as described herein is meant a polypeptide that binds BLyS, but does not necessarily comprise an identical or similar amino acid sequence of a BLyS binding polypeptide specified herein. BLyS binding polypeptides of the invention which are variants of a BLyS binding polypeptide specified herein satisfy at least one of the following: (a) a polypeptide comprising, or alternatively consisting of, an amino acid sequence that is at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95% least 99%, or 100% identical to the amino acid sequence of a BLyS binding polypeptide sequence disclosed herein

(SEQ ID NOs: 1-12, 20-172, and 186-444), (b) a polypeptide encoded by a nucleotide sequence, the complementary sequence of which hybridizes under stringent conditions to a nucleotide sequence encoding a BLyS binding polypeptide disclosed herein (e.g., a nucleic acid sequence encoding the amino acid sequence of SEQ ID NOs: 1-12, 20-172, and 186-444), and/or a fragment of a BLyS binding polypeptide disclosed herein, of at least 5 amino acid residues, at least 10 amino acid residues, at least 15 amino acid residues, or at least 20 amino acid residues. BLyS binding polypeptides of the invention also encompass polypeptide sequences that have been modified for various applications provided that such modifications do not eliminate the ability to bind a BLyS target. Specific, non-limiting examples of modifications contemplated include C-terminal or N-terminal amino acid substitutions or peptide chain elongations for the purpose of linking the BLyS binder to a chromatographic material or other solid support. Other substitutions contemplated herein include substitution of one or both of a pair of cysteine residues that normally form disulfide links, for example with non-naturally occurring amino acid residues having reactive side chains, for the purpose of forming a more stable bond between those amino acid positions than the former disulfide bond. All such modified binding polypeptides are also considered BLyS binding polypeptides according to this invention so long as the modified polypeptides retain the ability to bind BLyS and/or BLyS-like polypeptides, and therefore, may be used in one or more of the various methods described herein, such as, to detect, purify, or isolate BLyS or BLyS-like polypeptides in or from a solution. BLyS binding polypeptides of the invention also include variants of the specific BLyS binding polypeptide sequences disclosed herein (e.g., SEQ ID NOs: 1-12, 20-172, and 186-444) which have an amino acid sequence corresponding to one of these polypeptide sequences, but in which the polypeptide sequence is altered by substitutions, additions or deletions that provide for molecules that bind BLyS. Thus, the BLyS binding polypeptides include polypeptides containing, as a primary amino acid sequence, all or part of the particular BLyS binding polypeptide sequence including altered sequences in which functionally equivalent amino acid residues are substituted for residues within the sequence, resulting in a peptide which is functionally active. For example, one or more amino acid residues within the sequence can be substituted by another amino acid of a similar polarity which acts as a functional equivalent, resulting in a silent alteration. Conservative substitutions for an amino acid within the sequence may be selected from other members of the class to which the amino acid belongs. For example, the nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid. Such BLyS binding polypeptides can be made either by chemical peptide synthesis or by recombinant production from a nucleic acid encoding the BLyS binding polypeptide which nucleic acid has been mutated. Any technique for mutagenesis known in the art can be used, including but not limited to, chemical mutagenesis, in vitro site-directed mutagenesis (Hutchinson et al., J. Biol. Chem., 253:6551 (1978)), use of TAB.RTM. linkers (Pharmacia), etc.

PGPUB-DOCUMENT-NUMBER: 20030157677

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030157677 A1

TITLE: Mutants of Mycobacterium vaccae-derived formate dehydrogenase and uses thereof

PUBLICATION-DATE: August 21, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Mitsuhashi, Kazuya	Niigata		JP	
Yamamoto, Hiroaki	Ibaraki		JP	
Kimoto, Norihiro	Ibaraki		JP	

APPL-NO: 09/ 996008

DATE FILED: November 28, 2001

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
JP	2000-363894	2000JP-2000-363894	November 29, 2000
JP	2001-254631	2001JP-2001-254631	August 24, 2001

US-CL-CURRENT: 435/189, 435/135 , 435/254.2 , 435/320.1 , 435/69.1 , 536/23.2

ABSTRACT:

An objective of the present invention is to provide polypeptides capable of retaining a strong enzyme activity of formate dehydrogenase in the presence of an organic solvent and to provide the uses thereof.
Formate dehydrogenase mutant polypeptides, which are resistant to organic solvents, were constructed by substituting cysteines at position 146 and/or at position 256 in the amino acid sequence of Mycobacterium vaccae-derived formate dehydrogenase by site-directed mutagenesis. The polypeptides have strong activities of formate dehydrogenase in the presence of an organic solvent. The mutants are useful for the production of alcohols using ketones as raw material, etc.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (8):

[0006] Tishkov et al. have shown that mutants of formate dehydrogenase from Pseudomonas sp. 101, in which the cysteine at position 256 has been substituted with serine or methionine by site-directed mutagenesis, have enhanced stability to mercury but reduced thermal stability (Biochem. Biophys. Res. Commun. 192:4480-4485, 1993). They have also reported mutants showing enhanced thermal stability, which were similarly created by substituting serine with alanine, valine, or leucine at position 131, 160, 168, 184, or 228 (FEBS Letters 445:183-188, 1999).

PGPUB-DOCUMENT-NUMBER: 20030157645

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030157645 A1

TITLE: Subtilisin variants with improved characteristics

PUBLICATION-DATE: August 21, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kettling, Ulrich	Koeln		DE	
Koltermann, Andre	Koeln		DE	
Kensch, Oliver	Koeln		DE	
Kuhlemann, Rene	Koeln		DE	
Haupts, Ulrich	Koeln		DE	
Rarbach, Markus	Koeln		DE	
Odendahl, Konrad	Koeln		DE	

APPL-NO: 10/ 324152

DATE FILED: December 19, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60343056 20011221 US

US-CL-CURRENT: 435/69.1, 435/222 , 435/252.3 , 435/320.1 , 510/226 , 510/320 , 536/23.2

ABSTRACT:

The present invention provides subtilisin variants with improved characteristics, including improved substrate affinity, catalytic activity, catalytic efficiency and stability under washing conditions as well as overall wash performance. The subtilisin variants are therefore useful additives in cleaning compositions.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (5):

[0003] Properties of a protease can be improved by introducing mutations into the amino acid sequence of a precursor, subtilisin at defined positions. Such efforts have lead to better subtilisins as disclosed in several patent applications. For example, U.S. Pat. No. 5,346,823 describes subtilisin derivatives which are modified by substitution of methionine, trypthophane, lysine or cysteine with alanine or serine resulting in improved stability under highly oxidizing conditions.

PGPUB-DOCUMENT-NUMBER: 20030138894

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030138894 A1

TITLE: Methods and compositions for modulating ACE-2 activity

PUBLICATION-DATE: July 24, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Parry, Tom J.	Walkersville	MD	US	
Sekut, Les	Ijamsville	MD	US	
Rosen, Craig A.	Laytonsville	MD	US	
Albert, Vivian R.	Rockville	MD	US	
Sanyal, Indrajit	Bethesda	MD	US	
Huang, Lili	Burlington	MA	US	
Wescott, Charles R.	Belmont	MA	US	

APPL-NO: 10/ 158825

DATE FILED: June 3, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60294976 20010604 US

US-CL-CURRENT: 435/69.1, 435/226 , 435/320.1 , 435/325 , 514/12 , 530/324

ABSTRACT:

Binding polypeptides comprising specific amino acid sequences are disclosed that specifically bind ACE-2 protein or ACE-2-like polypeptides. The binding polypeptides can be used in methods of the invention for detecting, isolating, or purifying ACE-2 protein or ACE-2-like polypeptides in solutions or mixtures, or biological samples. The invention also relates to nucleic acid molecules encoding these ACE-2 binding polypeptides, vectors and host cells containing these nucleic acids, and methods for producing the same. The present invention also relates to methods and compositions for detecting, diagnosing, prognosing, preventing, treating or ameliorating a disease or disorder associated with aberrant ACE-2 or ACE-2 receptor expression or inappropriate function of ACE-2 or ACE-2 receptor, comprising use of ACE-2 binding polypeptides or fragments or variants thereof, that specifically bind to ACE-2.

[0001] This application claims benefit under 35 U.S.C. .sctn.119(e) of U.S. Patent Application No. 60/294,976, filed Jun. 4, 2001, which is hereby incorporated by reference in its entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (10):

[0149] A "ACE-2 binding polypeptide" is a molecule of the invention that can bind an ACE-2 target protein. Non-limiting examples of ACE-2 binding polypeptides of the invention are the polypeptide molecules having an amino

acid sequence described herein (see SEQ ID NOs: 1-136). The term ACE-2 binding polypeptide also encompasses ACE-2 binding fragments and variants (including derivatives) of polypeptides having the specific amino acid sequences described herein (SEQ ID NOs: 1-136). By "variant" of an amino acid sequence as described herein is meant a polypeptide that binds ACE-2, but does not necessarily comprise an identical or similar amino acid sequence of an ACE-2 binding polypeptide specified herein. ACE-2 binding polypeptides of the invention which are variants of an ACE-2 binding polypeptide specified herein satisfy at least one of the following: (a) a polypeptide comprising, or alternatively consisting of, an amino acid sequence that is at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, least 99%, or 100% identical to the amino acid sequence of an ACE-2 binding polypeptide sequence disclosed herein (SEQ ID NOs: 1-136), (b) a polypeptide encoded by a nucleotide sequence, the complementary sequence of which hybridizes under stringent conditions to a nucleotide sequence encoding an ACE-2 binding polypeptide disclosed herein (e.g., a nucleic acid sequence encoding the amino acid sequence of SEQ ID NOs: 1-136), and/or a fragment of an ACE-2 binding polypeptide disclosed herein, of at least 5 amino acid residues, at least 10 amino acid residues, at least 15 amino acid residues, or at least 20 amino acid residues. ACE-2 binding polypeptides of the invention also encompass polypeptide sequences that have been modified for various applications provided that such modifications do not eliminate the ability to bind an ACE-2 target. Specific, non-limiting examples of modifications contemplated include C-terminal or N-terminal amino acid substitutions or peptide chain elongations for the purpose of linking the ACE-2 bindor to a chromatographic material or other solid support. Other substitutions contemplated herein include substitution of one or both of a pair of cysteine residues that normally form disulfide links, for example with non-naturally occurring amino acid residues having reactive side chains, for the purpose of forming a more stable bond between those amino acid positions than the former disulfide bond. All such modified binding polypeptides are also considered ACE-2 binding polypeptides according to this invention so long as the modified polypeptides retain the ability to bind ACE-2 and/or ACE-2-like polypeptides, and therefore, may be used in one or more of the various methods described herein, such as, to detect, purify, or isolate ACE-2 or ACE-2-like polypeptides in or from a solution. ACE-2 binding polypeptides of the invention also include variants of the specific ACE-2 binding polypeptide sequences disclosed herein (e.g., SEQ ID NOs: 1-136) which have an amino acid sequence corresponding to one of these polypeptide sequences, but in which the polypeptide sequence is altered by substitutions, additions or deletions that provide for moleucles that bind ACE-2. Thus, the ACE-2 binding polypeptides include polypeptides containing, as a primary amino acid sequence, all or part of the particular ACE-2 binding polypeptide sequence including altered sequences in which functionally equivalent amino acid residues are substituted for residues within the sequence, resulting in a peptide which is functionally active. For example, one or more amino acid residues within the sequence can be substituted by another amino acid of a similar polarity which acts as a functional equivalent, resulting in a silent alteration. Conservative substitutions for an amino acid within the sequence may be selected from other members of the class to which the amino acid belongs. For example, the nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid. Such ACE-2 binding polypeptides can be made either by chemical peptide synthesis or by recombinant production from a nucleic acid encoding the ACE-2 binding polypeptide which nucleic acid has been

mutated. Any technique for mutagenesis known in the art can be used, including but not limited to, chemical mutagenesis, in vitro site-directed mutagenesis (Hutchinson et al., J. Biol. Chem., 253:6551 (1978)), use of TAB.RTM. linkers (Pharmacia), etc.

US-PAT-NO: 6713284

DOCUMENT-IDENTIFIER: US 6713284 B2

TITLE: Bacterial superantigen vaccines

DATE-ISSUED: March 30, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ulrich; Robert G.	Frederick	MD	N/A	N/A
Olson; Mark A.	Gaithersburg	MD	N/A	N/A
Bavari; Sina	Dillsburg	PA	N/A	N/A

APPL-NO: 08/ 882431

DATE FILED: June 25, 1997

US-CL-CURRENT: 435/69.3, 435/252.3 , 435/252.33 , 435/320.1 , 435/325 , 435/69.1 , 435/71.1 , 435/71.3 , 536/23.1 , 536/23.7

ABSTRACT:

The present invention relates to genetically attenuated superantigen toxin vaccines altered such that superantigen attributes are absent, however the superantigen is effectively recognized and an appropriate immune response is produced. The attenuated superantigen toxins are shown to protect animals against challenge with wild type toxin. Methods of producing and using the altered superantigen toxins are described.

30 Claims, 12 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 8

---------- KWIC ---------

Detailed Description Text - DETX (9):

The binding interface between SEB and HLA-DR1 consists principally of two structurally conserved surfaces located in the N-terminal domain: a polar binding pocket derived from three .beta.-strand elements of the .beta.-barrel domain and a hydrophobic reverse turn. The binding pocket of SEB contains residues E67 (E=Glutamic acid), Y89 (Y=Tyrosine) and Y115 (Y=tyrosine), and binds K39 (K=Lysine) of the DR.alpha. subunit. The amino acid one letter code is defined as the following: A=Alanine (Ala), I=Isoleucine (Ile), L=Leucine (Leu), M=Methionine (Met), F=Phenylalanine (Phe), P=Proline (Pro), W=Tryptophan (Trp), V=Valine (Val), N=Asparagine (Asn), C=Cysteine (Cys), Q=Glutamine (Q), G=Glycine (Gly), S=Serine (Ser), T=Threonine (Thr), Y=Tyrosine (Tyr), R=Arginine (Arg), H=Histidine (His), K=Lysine (Lys), D=Aspartic acid (Asp), and E=Glutamic acid (Glu). For SEA, the binding interface with the DR molecule is modeled to contain a similar binding pocket consisting of residues D70, Y92 and Y108. Mutation of residue Y89 in SEB or Y92 in SEA to alanine (FIG. 2) resulted in greater than 100-fold reduction in DR1 binding. The substitution of alanine for Y89 in SEB and Y92 in SEA eliminates the hydrogen bond with K39 and disrupts packing interactions with adjacent protein residues. Modeling of

the SEA mutant Y92A predicts an increase in solvent-accessible surface area for Y108 by a factor of two greater than the wild-type structure, allowing the formation of a hydrogen bond to the carboxylate group of D70 and thus disrupting key anchoring and recognition points for HLA-DR1. This effect is expected to be somewhat less in SEB due to the longer side chain at E67. Substitution of SEB Y115 with alanine also resulted in greater than 100-fold reduction of binding. In contrast, the same replacement of Y108 in SEA yielded little to no change in DR1 binding (FIG. 2a), suggesting the primary importance of SEA residues Y92 and D70 for stabilizing interactions with K39. The K39 side chain of DR.alpha. forms a strong ion-pair interaction with the SEB E67 carboxylate group and hydrogen bonds with the hydroxyl groups of Y89 and Y115. Substitution of SEB E67 by glutamine reduced binding affinity by greater than 100-fold (FIG. 2), reflecting the replacement of the strong ionic bond with a weaker hydrogen bond. To optimize ion-pair interactions of the analogous SEA site, the shorter carboxylate side chain of D70 is predicted to shift K39 of DR.alpha., weakening interactions with SEA Y108. The substitution of alanine for SEA Y108 is thus more easily accommodated than the homologous substitution of SEB Y115, without loss in DR1 binding.

US-PAT-NO: 6713276

DOCUMENT-IDENTIFIER: US 6713276 B2

TITLE: Modulation of A.beta. levels by .beta.-secretase BACE2

DATE-ISSUED: March 30, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cordell; Barbara	Palo Alto	CA	N/A	N/A
Schimmoller; Frauke	Menlo Park	CA	N/A	N/A
Liu; Yu-Wang	Santa Clara	CA	N/A	N/A
Quon; Diana Hom	Redwood City	CA	N/A	N/A

APPL-NO: 09/ 886143

DATE FILED: June 20, 2001

PARENT-CASE:

This application claims priority under 35 U.S.C. .sctn.119(e) to U.S. Provisional Application No. 60/215,729 filed Jun. 28, 2000.

US-CL-CURRENT: 435/23, 435/24 , 435/69.2

ABSTRACT:

The present invention is based on the findings that BACE 2, a homolog of .beta.-secretase BACE, is able to stimulate processing of APP in a non-amyloidogenic pathway, thereby suppressing the level of A.beta.. Accordingly, the present invention provides methods and means for the identification and use of modulators of this unique activity of BACE 2 to suppress A.beta. production. The compounds identified using the methods and means provided herein may be used as potential candidates for the treatment of Alzheimer's disease and other neurological diseases.

27 Claims, 8 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 8

---------- KWIC ---------

Detailed Description Text - DETX (119):

As described above, BACE2 expression resulted in the accumulation of APP CTFs concomitant with the reduction of A.beta. levels. This effect prompted investigation into whether .beta.-secretase cleavage was required for A.beta. suppression. The effects of BACE2 on the metabolism of the C-terminal 100 amino acids of APP (CT100), a construct that mimics prior .beta.-secretase cleavage (Shoji et al., Science 258: 126-129 [1992]), was analyzed. When CT100 was expressed in HEK293T cells, A.beta. levels were significantly increased over mock-transfected cells (FIG. 5A). As expected, additional BACE copies did not affect the levels of A.beta. under CT100overexpression conditions. Co-expression of BACE2 and CT100 resulted in the dramatic suppression of total

A.beta. as well as A.beta.42 levels (FIGS. 5a, b). Thus, the capacity of BACE2 to suppress A.beta. formation does not require prior .beta.-secretase cleavage. The dramatic reduction in A.beta. formation was confirmed by Western blotting of conditioned medium and the CTFs in the lysate (FIG. 5c). BACE2 also led to the accumulation of a fragment that corresponded in size to .alpha.-CTF. At steady-state, this was accompanied by a partial reduction in CT100 which corresponds to .beta.-CTF confirming that .beta.-CTF could be converted to .alpha.-CTF under these BACE2 conditions. To confirm that there was a precursor-product relationship between .beta.-CTF (i.e., CT100) and the .alpha.-like CTF that accumulated upon BACE2 overexpression, a pulse-chase analysis was performed. HEK293 cells were transfected with CT100 alone or CT100 with BACE2. Cells were readiolabeled with .sup.35 S-methionine/cysteine for 15 minutes after which the medium containing radiolabel was removed and replaced with standard medium. The cells were then incubated for 90 minutes. Over this 90-minute period, samples were taken and assessed for CTFs by immunoprecipitation. Under these CT100 transfection conditions, endogenous APP was negligible in the formation of CTFs. While CT100 was fairly stable in mock-transfected cells, BACE2 expression yielded a pattern of CTFs that was identical to that observed when APP was co-transfected (FIG. 5d). Again, BACE2 resulted in the accumulation of the .alpha.-like CTF, clearly indicating that it was derived from CT100. This effect was rescued when a critical aspartate residue was mutated in BACE2 (D110A in FIG. 5d; also see below). This indicates that BACE2 has .alpha.-secretase-like activity. Taken together, these data indicate that the ability of BACE2 to suppress A.beta. production reflects enhanced .alpha.-secretase-like activity that is independent of prior .beta.-secretase cleavage. This .alpha.-secretase-like activity of BACE2 promotes the non-amyloidogenic processing of APP or APP fragments and reduces the production of A.beta..

US-PAT-NO: 6693181

DOCUMENT-IDENTIFIER: US 6693181 B2

TITLE: Protein secretion

DATE-ISSUED: February 17, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ashkenazi; Avi J.	San Mateo	CA	N/A	N/A
Berman; Phillip W.	Portola Valley	CA	N/A	N/A
Brousseau; David	San Francisco	CA	N/A	N/A
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APPL-NO: 09/ 291925

DATE FILED: April 14, 1999

PARENT-CASE:

This application claims benefit of Prov. No. 60/082,002 filed Apr. 16, 1998 and claims benefit of Ser. No. 60/123,522 filed Mar. 8, 1999.

US-CL-CURRENT: 536/23.4, 435/69.1 , 435/69.8 , 435/70.1 , 530/350 , 536/23.5

ABSTRACT:

DNA constructs, host cells and production methods are disclosed for the expression and recovery of polypeptides, especially those altered to have one or more glycosylation sites added or deleted. The DNA constructs, host cells and methods provided herein employ a DNA segment corresponding to a mammalian tissue plasminogen activator signal and/or pro peptide.

13 Claims, 26 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 9

---------- KWIC ---------

Drawing Description Text - DRTX (5):

FIGS. 4A-4C. Immunoprecipitation of TNFR-IgG1 glycosylation mutants. Plasmids encoding either TNFR-IgG1 or TNFR-IgG glycosylation site mutants were transfected into 293 cells using calcium phosphate precipitated DNA. Two days post-transfection the culture, medium was removed and replaced (after washing two times) with methionine- and cysteine-free DMEM supplemented with (.sup.35 S)-labeled methionine and cysteine. Cells were labeled overnight at 37.degree. C. (5% CO.sub.2). Cell lysates and cell culture supernatants were precipitated by the addition of Protein A SEPHAROSE.TM.. The Protein A:TNFR-IgG1 complexes were pelleted by centrifugation, washed repeatedly and eluted in SDS-PAGE sample buffer containing mercaptoethanol. The eluted protein was resolved on 10% SDS-PAGE gels and visualized by autoradiography. The glycosylation site mutants were examined in four separate experiments (FIGS. 4A-4D) where transiently expressed TNFR-IgG1 (TNFR-IgG1) expressed in 293 cells or a stable

CHO cell line expressing TNFR-IgG (TRY+) were used as positive controls. Background binding was determined in experiments with cells transfected with thrombopoeitin (TPO-). The mobilities of molecular weight markers are indicated at the left margins.

US-PAT-NO: 6692917

DOCUMENT-IDENTIFIER: US 6692917 B2

TITLE: Systems and methods for invasive cleavage reaction on dendrimers

DATE-ISSUED: February 17, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Neri; Bruce P.	Madison	WI	N/A	N/A
Hall; Jeff G.	Madison	WI	N/A	N/A
Lyamichev; Victor	Madison	WI	N/A	N/A
Smith; Lloyd M.	Madison	WI	N/A	N/A

APPL-NO: 09/ 940244

DATE FILED: August 27, 2001

PARENT-CASE:

The present invention is a continuation-in-part of co-pending U.S. application Ser. No. 09/732,622, filed Dec. 8, 2000 which is a continuation-in-part of U.S. application Ser. No. 09/350,309 filed Jul. 9, 1999, U.S. Pat. No. 6,348,314, which is a divisional application of U.S. application Ser. No. 08/756,386, filed Nov. 26, 1996 U.S. Pat. No. 5,985,557; is also a continuation-in-part of co-pending U.S. application Ser. No. 09/381,212, filed Feb. 8, 2000 which is a national entry of PCT Appl. No. U.S. 98/05809, filed Mar. 24, 1998 which claims priority to U.S. Pat. Nos. 5,994,069, 6,090,543, 5,985,557, 6,001,567, and 5,846,717 and PCT Appln. No. U.S. 97/01072; each of which is hereby incorporated by reference in their entireties.

US-CL-CURRENT: 435/6, 536/24.3

ABSTRACT:

The present invention relates to compositions and methods for the detection and characterization of nucleic acid sequences and variations in nucleic acid sequences. The present invention relates to methods for forming a nucleic acid cleavage structure on dendrimers and cleaving the nucleic acid cleavage structure in a site-specific manner. For example, in some embodiments, a 5' nuclease activity from any of a variety of enzymes is used to cleave the target-dependent cleavage structure, thereby indicating the presence of specific nucleic acid sequences or specific variations thereof.

38 Claims, 238 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 210

---------- KWIC ---------

Detailed Description Text - DETX (238):

Some embodiments of the present invention provide mutant or variant forms of enzymes described herein. It is possible to modify the structure of a peptide having an activity of the enzymes described herein for such purposes as enhancing cleavage rate, substrate specificity, stability, and the like. For example, a modified peptide can be produced in which the amino acid sequence has been altered, such as by amino acid substitution, deletion, or addition. For example, it is contemplated that an isolated replacement of a leucine with an isoleucine or valine, an aspartate with a glutamate, a threonine with a serine, or a similar replacement of an amino acid with a structurally related amino acid (i.e., conservative mutations) will not have a major effect on the biological activity of the resulting molecule. Accordingly, some embodiments of the present invention provide variants of enzymes described herein containing conservative replacements. Conservative replacements are those that take place within a family of amino acids that are related in their side chains. Genetically encoded amino acids can be divided into four families: (1) acidic (aspartate, glutamate); (2) basic (lysine, arginine, histidine); (3) nonpolar (alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan); and (4) uncharged polar (glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine). Phenylalanine, tryptophan, and tyrosine are sometimes classified jointly as aromatic amino acids. In similar fashion, the amino acid repertoire can be grouped as (1) acidic (aspartate, glutamate); (2) basic (lysine, arginine histidine), (3) aliphatic (glycine, alanine, valine, leucine, isoleucine, serine, threonine), with serine and threonine optionally be grouped separately as aliphatic-hydroxyl; (4) aromatic (phenylalanine, tyrosine, tryptophan); (5) amide (asparagine, glutamine); and (6) sulfur-containing (cysteine and methionine) (See e.g., Stryer (ed.), Biochemistry, 2nd ed, W H Freeman and Co. [1981]). Whether a change in the amino acid sequence of a peptide results in a functional homolog can be readily determined by assessing the ability of the variant peptide to produce a response in a fashion similar to the wild-type protein using the assays described herein. Peptides in which more than one replacement has taken place can readily be tested in the same manner.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	441	methionine adj aminopeptidase$	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:38
L2	7079	(methionine or met) same muta$10	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:38
L3	185	1 same 2	US-PGPUB; USPAT	OR	OFF	2004/04/20 15:39
L4	1908	methionine same cysteine same muta$10	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:17
L5	102	4 same stab$8	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:18
L6	19342	oxidat$ near4 stab$8	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:25
L7	65	4 and 6	US-PGPUB; USPAT	OR	OFF	2004/04/20 16:26

PGPUB-DOCUMENT-NUMBER: 20040053390

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040053390 A1

TITLE: Computational method for designing enzymes for incorporation of non natural amino acids into proteins

PUBLICATION-DATE: March 18, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Datta, Deepshikha	South Pasadena	CA	US	
Wang, Pin	Pasadena	CA	US	
Carrico, Isaac	Pasadena	CA	US	
Mayo, Stephen L.	Pasadena	CA	US	
Tirrell, David	Pasadena	CA	US	

APPL-NO: 10/ 375298

DATE FILED: February 27, 2003

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60360146 20020227 US

US-CL-CURRENT: 435/199, 435/320.1 , 435/325 , 435/69.1 , 702/19

ABSTRACT:

The instant invention provides methods, reagents, and computational tools for designing non-natural substrate analogs for enzymes, especially for designing unnatural amino acid analogs for aminoacyl tRNA Synthetases (AARSs), such as the Phe tRNA Synthetase. The instant invention also provides methods to incorporate unnatural amino acid analogs, especially those with interesting functional groups, into protein products to generate proteins of modified or novel functions.

REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit under 35 U.S.C. 119(e) of U.S. Provisional Application No. 60/360,146, filed on Feb. 27, 2002, the entire content of which is incorporated herein by reference.

---------- KWIC ---------

Detail Description Paragraph - DETX (213):

[0243] Once made, the designed AARS proteins are experimentally evaluated and tested for structure, altered function and stability, as necessary. This will be done as is known in the art, and will depend in part on the original protein from which the protein backbone structure was taken. Preferably, the designed AARS proteins are more stable than the known AARS protein that was used as the starting point, although in some cases, if some constaints are placed on the methods, the designed protein may be less stable. Thus, for example, it is possible to fix certain residues for altered biological activity and find the most stable sequence, but it may still be less stable than the

wild type protein. Stable in this context means that the new protein retains either biological activity or conformation past the point at which the parent molecule did. Stability includes, but is not limited to, thermal stability, i.e. an increase in the temperature at which reversible or irreversible denaturing starts to occur; proteolytic stability, i.e. a decrease in the amount of protein which is irreversibly cleaved in the presence of a particular protease (including autolysis); stability to alterations in pH or oxidative conditions; chelator stability; stability to metal ions; stability to solvents such as organic solvents, surfactants, formulation chemicals; etc.

Detail Description Paragraph - DETX (273):

[0302] The crystal structure of Thermus thermophilus PheRS (tPheRS) complexed with t is available.sup.9 and there is 43% overall sequence identity between ePheRS and /PheRS; sequence identity in the identified active site region is 80%. We therefore employed a previously described protein design algorithm.sup.10 to identify potentially useful mutants of tPheRS, with the intention to prepare and evaluate the corresponding mutant forms of ePheRS. We generated a backbone-independent rotamer library for 2, in which both the .chi..sub.1 and .chi..sub.2 torsional angles were varied by .+-.20.degree. (in increments of 5.degree.) from the values of 1 in the tPheRS structure. Design calculations were performed by fixing the identity of the substrate (2) and by allowing each of 11 non-anchor sites in the amino acid binding pocket of tPheRS (determined from the crystal structure) to be occupied by any of the twenty natural amino acids except for proline, methionine and cysteine. The anchor residues (Glu128, Glu130, Trp149, His178, Ser180, Gln183, and Arg204) were held fixed in identity and conformation in all calculations. These residues contribute important electrostatic interactions with the substrate and it is reasonable to assume that such interactions are equally critical for the binding of 2.

Detail Description Paragraph - DETX (307):

[0336] Design calculations were run by fixing the identity of the substrate to be DPA and varying 11 other positions on PheRS (137, 184, 187, 222, 258, 260, 261, 286, 290, 294, and 314). Positions 137, 184, 258, 260, 261, 286, 290, 294, 314 were allowed to be any of the 20 natural amino acids except proline (Pro or P), methionine (Met or M) and cysteine (Cys or C). Methionine was allowed at position 187 because its wild-type identity is Met, and only hydorphobic amino acids were allowed at position 222. Most of these positions are buried in the core and a number of them pack against Phe in the crystal structure. Mutation analysis at position 294 has been shown to alter substrate specificity. The anchor residues (Glu 128, Glue 130, Trp 149, His 178, Ser 180, Gln 183, Arg 204) were held fixed both in identity and conformation in all the calculations. These make very important electrostatic interactions with the substrate and this interaction is probably equally critical for the analogs. From the crystal structure it appears that the anchor residues hold the Phe zwitterion in a way that the carbonyl group of the zwitterion is close to the ATP binding site. This proximity may be important for the aminoadenylation reaction. The aminoadenylation step is required for the incorporation of all the amino acids and hence, it seems important to make sure that the carbonyl and the amide groups of the analog zwitterions are also anchored the same way as the natural substrate at this site.

PGPUB-DOCUMENT-NUMBER: 20040029174

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040029174 A1

TITLE: End selection in directed evolution

PUBLICATION-DATE: February 12, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Short, Jay M.	Rancho Santa Fe	CA	US	
Frey, Gerhard Johann	San Diego	CA	US	

US-CL-CURRENT: 435/7.1, 435/69.1 , 530/350

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of end-selection-based methods is the ability to recover full-length polynucleotides from a library of progeny molecules generated by mutagenesis methods. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

PGPUB-DOCUMENT-NUMBER: 20040013667

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040013667 A1

TITLE: Treatment with anti-ErbB2 antibodies

PUBLICATION-DATE: January 22, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kelsey, Stephen M.	Montara	CA	US	
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APPL-NO: 10/ 608626

DATE FILED: June 27, 2003

RELATED-US-APPL-DATA:

child 10608626 A1 20030627

parent continuation-in-part-of 10268501 20021010 US PENDING

child 10268501 20021010 US

parent continuation-in-part-of 09602812 20000623 US PENDING

non-provisional-of-provisional 60141316 19990625 US

US-CL-CURRENT: 424/143.1, 424/141.1

ABSTRACT:

The present application describes methods for treating cancer with anti-ErbB2 antibodies, such as anti-ErbB2 antibodies that block ligand activation of an ErbB receptor.

RELATED APPLICATIONS

[0001] This application is a continuation-in-part of U.S. Ser. No. 10/268,501 filed Oct. 10, 2002, which is a continuation-in-part of U.S. Ser. No. 09/602,812 filed Jun. 23, 2000, which is a non-provisional application filed under 37 CFR 1.53(b)(1), claiming priority under 35 USC 119(e) to provisional application No. 60/141,316 filed Jun. 25, 1999, the contents of both applications are incorporated herein by reference.

---------- KWIC ---------

Brief Description of Drawings Paragraph - DRTX (2):

[0030] FIGS. 1A and 1B depict epitope mapping of residues 22-645 within the extracellular domain (ECD) of ErbB2 (amino acid sequence, including signal sequence, shown in FIG. 1A; SEQ ID NO:13) as determined by truncation mutant analysis and site-directed mutagenesis (Nakamura et al. J. of Virology 67(10):6179-6191 (1993); and Renz et al. J. Cell Biol. 125(6):1395-1406

(1994)). The various ErbB2-ECD truncations or point mutations were prepared from cDNA using polymerase chain reaction technology. The ErbB2 mutants were expressed as gD fusion proteins in a mammalian expression plasmid. This expression plasmid uses the cytomegalovirus promoter/enhancer with SV40 termination and polyadenylation signals located downstream of the inserted cDNA. Plasmid DNA was transfected into 293 cells. One day following transfection, the cells were metabolically labeled overnight in methionine and cysteine-free, low glucose DMEM containing 1% dialyzed fetal bovine serum and 25 .mu.Ci each of .sup.35S methionine and .sup.35S cysteine. Supernatants were harvested and either the anti-ErbB2 monoclonal antibodies or control antibodies were added to the supernatant and incubated 24 hours at 4.degree. C. The complexes were precipitated, applied to a 10-20% Tricine SDS gradient gel and electrophoresed at 100 V. The gel was electroblotted onto a membrane and analyzed by autoradiography. As shown in FIG. 1B, the anti-ErbB2 antibodies 7C2, 7F3, 2C4, 7D3, 3E8, 4D5, 2H11 and 3H4 bind various ErbB2 ECD epitopes.

Detail Description Paragraph - DETX (139):

[0180] Any cysteine residue not involved in maintaining the proper conformation of the anti-ErbB2 antibody also may be substituted, generally with serine, to improve the oxidative stability of the molecule and prevent aberrant crosslinking. Conversely, cysteine bond(s) may be added to the antibody to improve its stability (particularly where the antibody is an antibody fragment such as an Fv fragment).

PGPUB-DOCUMENT-NUMBER: 20030194763

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030194763 A1

TITLE: End selection in directed evolution

PUBLICATION-DATE: October 16, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Short, Jay M.	Encinitas	CA	US	
Frey, Gerhard Johann	San Diego	CA	US	

US-CL-CURRENT: 435/69.1, 435/183 , 435/252.3 , 435/270 , 435/320.1 , 435/325 , 435/6 , 435/7.1 , 435/91.1 , 435/91.2 , 436/501 , 514/1 , 530/350 , 536/23.1 , 536/23.2 , 536/23.4 , 536/23.5 , 536/24.33

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of end-selection-based methods is the ability to recover full-length polynucleotides from a library of progeny molecules generated by mutagenesis methods. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

PGPUB-DOCUMENT-NUMBER: 20030143220

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030143220 A1

TITLE: Hybrid immunoglobulins

PUBLICATION-DATE: July 31, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Capon, Daniel J.	San Mateo	CA	US	
Lasky, Laurence A.	Sausalito	CA	US	

APPL-NO: 10/ 097044

DATE FILED: March 12, 2002

RELATED-US-APPL-DATA:

child 10097044 A1 20020312

parent continuation-of 08906549 19970805 US GRANTED

parent-patent 6406697 US

child 08906549 19970805 US

parent continuation-of 08451848 19950526 US GRANTED

parent-patent 5714147 US

child 08451848 19950526 US

parent continuation-of 08185670 19940121 US GRANTED

parent-patent 5514582 US

child 08185670 19940121 US

parent continuation-of 07986931 19921208 US GRANTED

parent-patent 5428130 US

child 07986931 19921208 US

parent continuation-of 07808122 19911216 US GRANTED

parent-patent 5225538 US

child 07808122 19911216 US

parent division-of 07440625 19891122 US GRANTED

parent-patent 5116964 US

child 07440625 19891122 US

parent continuation-in-part-of 07315015 19890223 US GRANTED

parent-patent 5098833 US

US-CL-CURRENT: 424/130.1

ABSTRACT:

Novel polypeptides are provided, together with methods for making and using them, and nucleic acids encoding them. These polypeptides are useful as cell surface adhesion molecules and ligands, and are useful in therapeutic or diagnostic compositions and methods.

[0001] This is a Continuation-In-Part of U.S. Ser. No. 07/315,015, filed Feb. 23, 1989.

---------- KWIC ---------

Detail Description Paragraph - DETX (78):
[0120] Deletions of cysteine or other labile residues also may be desirable, for example in increasing the oxidative stability of the LHR. Deletion or substitutions of potential proteolysis sites, e.g. Arg Arg, is accomplished by deleting one of the basic residues or substituting one by glutaminyl or histidyl residues.

Detail Description Paragraph - DETX (224):
[0257] Correct mutants were tested for expression by transfection onto human kidney 293 cells using previously described methods. 35S methionine and cysteine labeled supernatants were analyzed by immunoprecipitation with protein A sepharose beads in the absence of added antibodies. The precipitated proteins were analyzed on 7 5% polyacrylamide-SDS gels either with or without reduction with beta mercaptoethanol. Plasmids that resulted in correctly expressed chimeras were introduced into 293 cells by transfection in the presence of selective plasmids encoding resistance to G418 as well as dihydrofolate reductase. Clones were selected in G418, and the incorporated plasmids were amplified in the presence of methotrexate. Permanent cell lines expressing high levels of each construct were grown to large scale in T-flasks, and the cell supernatants were clarified by centrifugation and filtration. The resultant supernatants were concentrated by Amicon filtration and passed over standard protein A-sepharose columns, washed with PBS and eluted with 0.1M Acetic Acid, 0.15 M NaCl (pH 3.5). The eluted material was immediately neutralized with 3 M Tris, pH 9, and quantitated by SDS gel electrophoresis as well as an ELISA assay

US-PAT-NO: 6713282

DOCUMENT-IDENTIFIER: US 6713282 B2

TITLE: End selection in directed evolution

DATE-ISSUED: March 30, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA	N/A	N/A
Frey; Gerhard Johann	San Diego	CA	N/A	N/A

US-CL-CURRENT: 435/69.1, 435/6

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of end-selection-based methods is the ability to recover full-length polynucleotides from a library of progeny molecules generated by mutagenesis methods. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

29 Claims, 11 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 7

US-PAT-NO: 6713279

DOCUMENT-IDENTIFIER: US 6713279 B1

TITLE: Non-stochastic generation of genetic vaccines and enzymes

DATE-ISSUED: March 30, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA	N/A	N/A

US-CL-CURRENT: 435/69.1, 435/320.1 , 435/334 , 435/6

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by use of non-stochastic methods of directed evolution (DirectEvolution.TM.). These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). Through use of the claimed methods, genetic vaccines, enzymes, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

105 Claims, 73 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 64

US-PAT-NO: 6635449

DOCUMENT-IDENTIFIER: US 6635449 B2

TITLE: Exonuclease-mediated nucleic acid reassembly in directed evolution

DATE-ISSUED: October 21, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA	N/A	N/A

US-CL-CURRENT: 435/69.1, 530/350 , 536/23.2

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of exonuclease-mediated reassembly methods is the ability to reassemble nucleic acid strands that would otherwise be problematic to chimerize. Exonuclease-mediated reassembly methods can be used in combination with other mutagenesis methods provided herein. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

17 Claims, 6 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 6